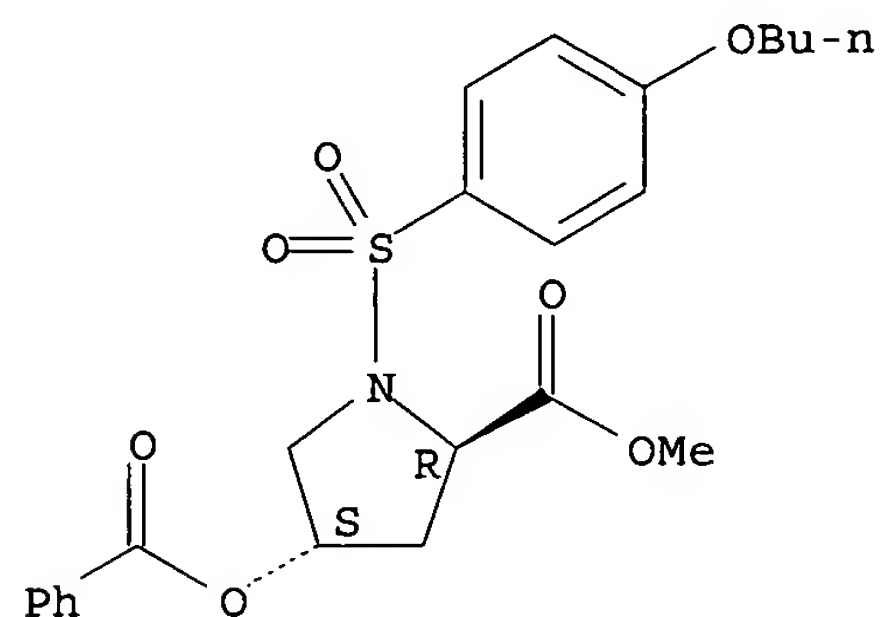


RN 204072-49-1 HCAPLUS

CN D-Proline, 4-(benzoyloxy)-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester,  
(4S)- (9CI) (CA INDEX NAME)

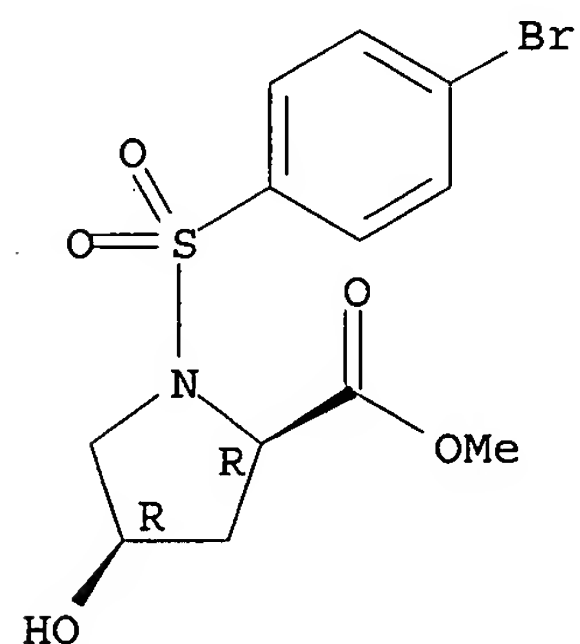
Absolute stereochemistry.



RN 204072-50-4 HCAPLUS

CN D-Proline, 1-[(4-bromophenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

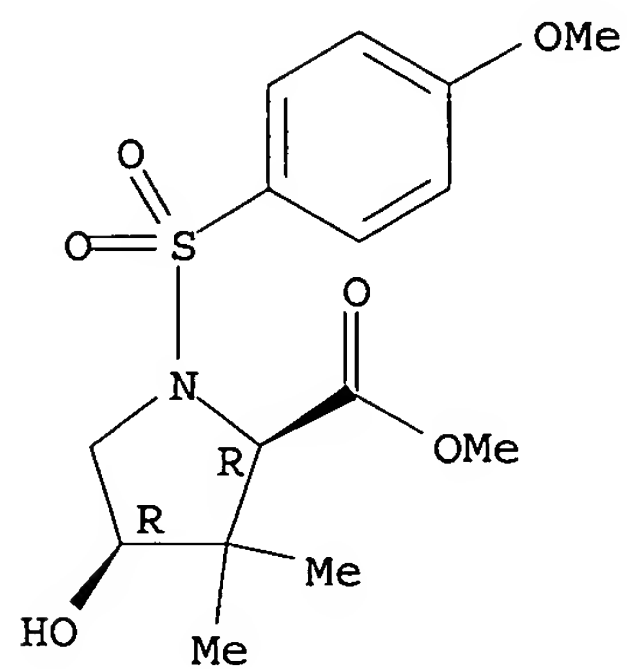


RN 204072-51-5 HCAPLUS

CN D-Proline, 1-[(4-bromo-2-methylphenyl)sulfonyl]-4-hydroxy-, methyl ester,  
(4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

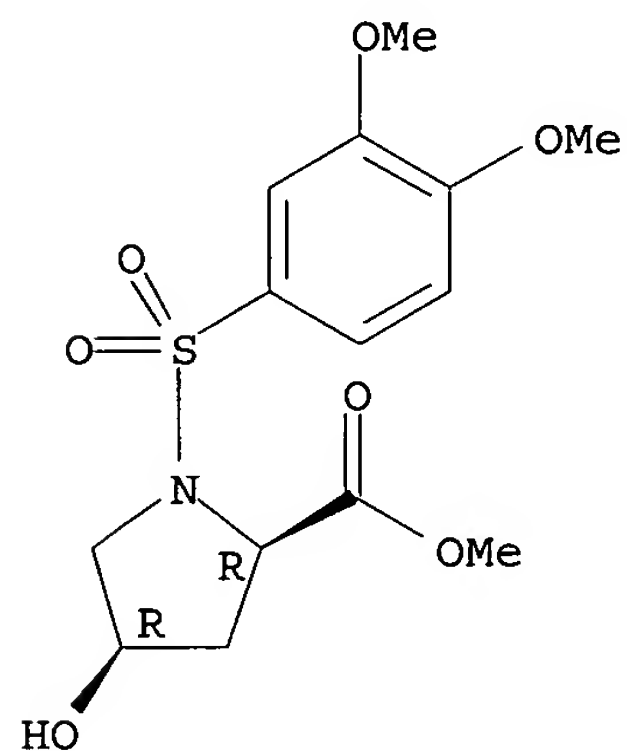
Absolute stereochemistry.



RN 204072-46-8 HCAPLUS

CN D-Proline, 1-[(3,4-dimethoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester,  
(4R) - (9CI) (CA INDEX NAME)

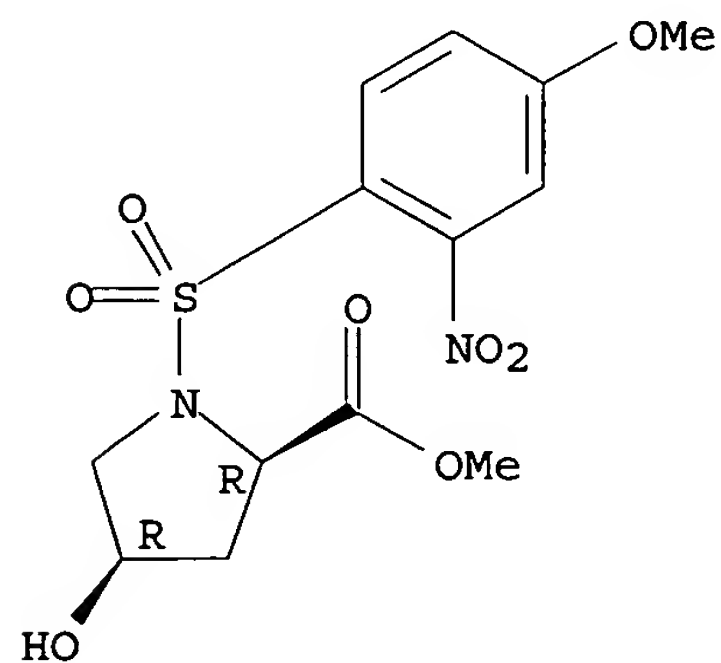
Absolute stereochemistry.



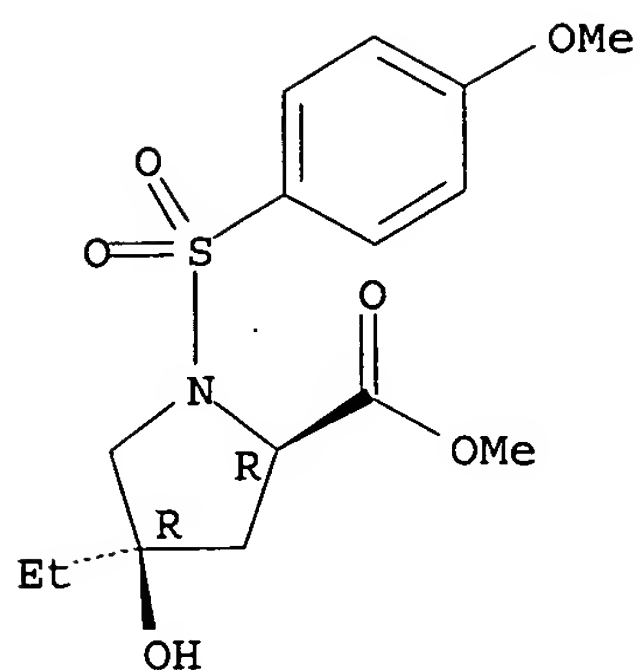
RN 204072-47-9 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methoxy-2-nitrophenyl)sulfonyl]-, methyl ester,  
(4R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

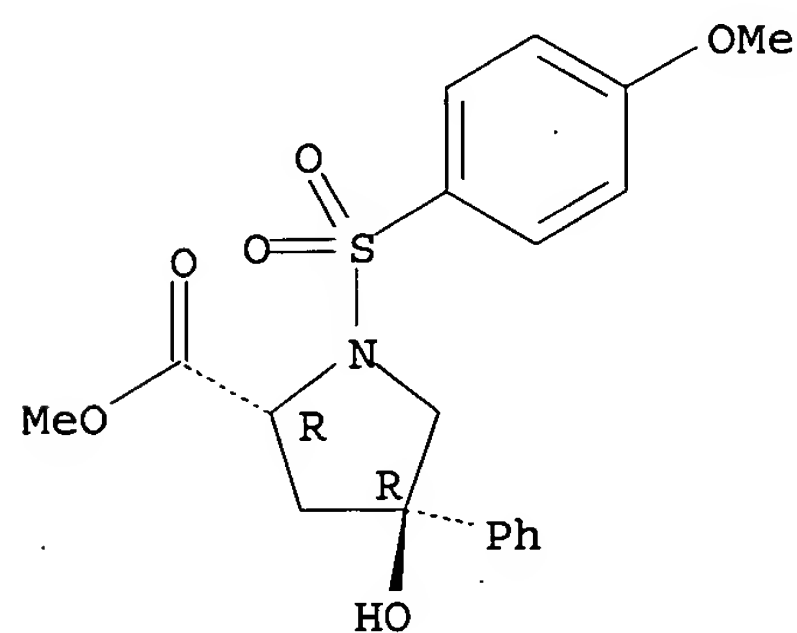






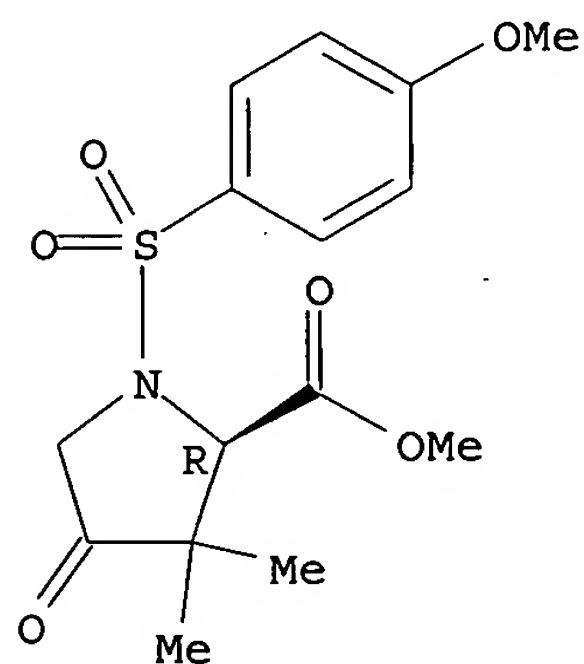
RN 204072-42-4 HCAPLUS  
 CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-phenyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

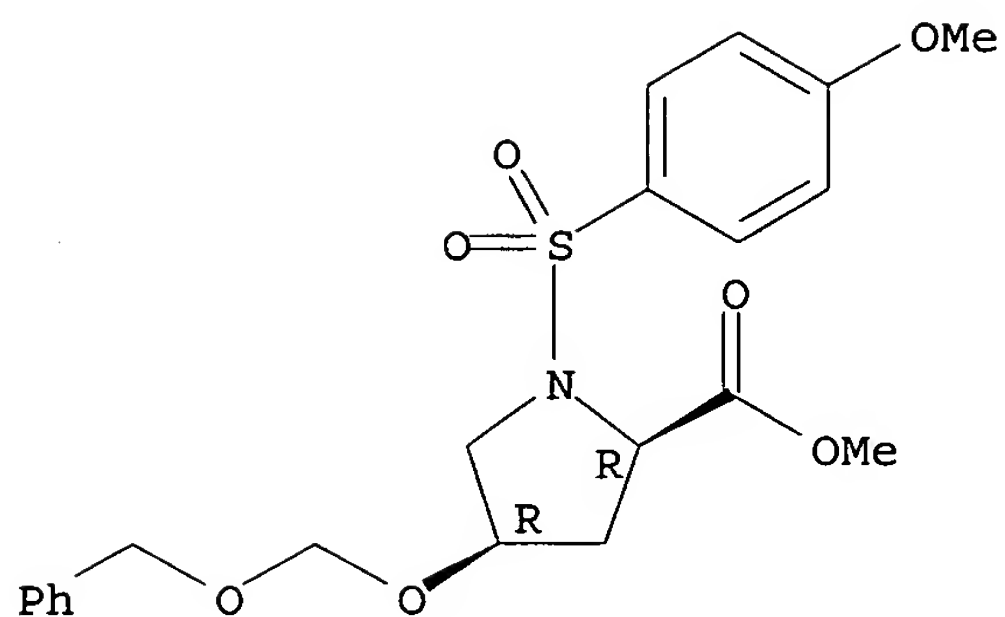


RN 204072-44-6 HCAPLUS  
 CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



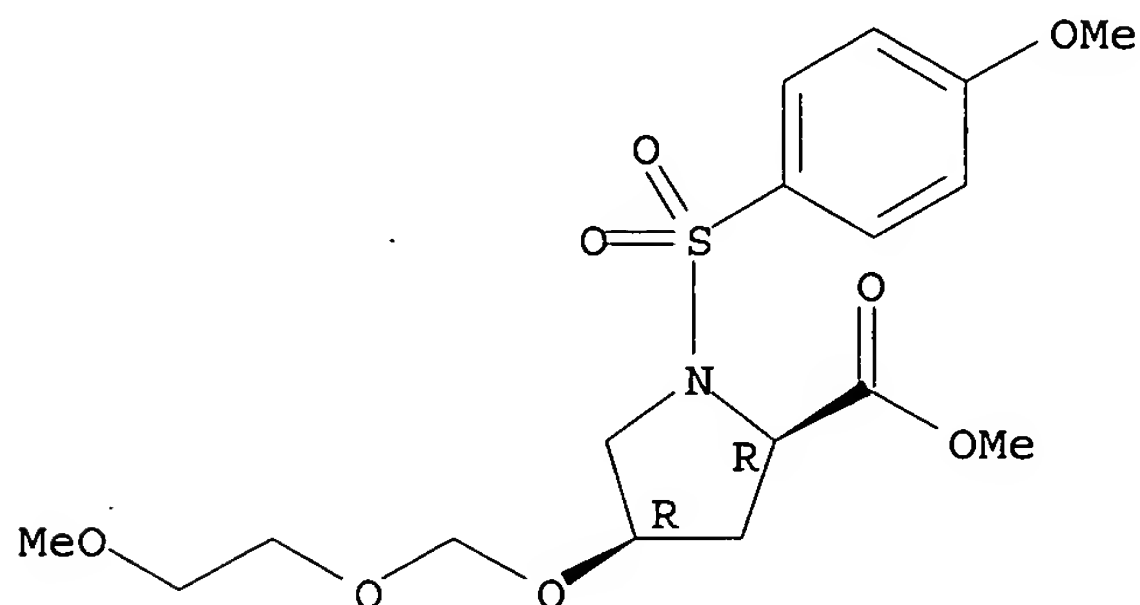
RN 204072-45-7 HCAPLUS  
 CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)



RN 204072-38-8 HCAPLUS

CN D-Proline, 4-[(2-methoxyethoxy)methoxy]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

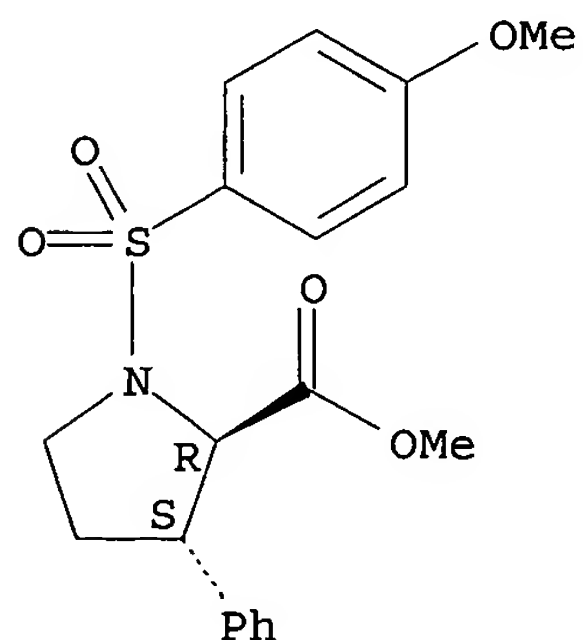
Absolute stereochemistry.



RN 204072-39-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-3-phenyl-, methyl ester, (3S)-rel- (9CI) (CA INDEX NAME)

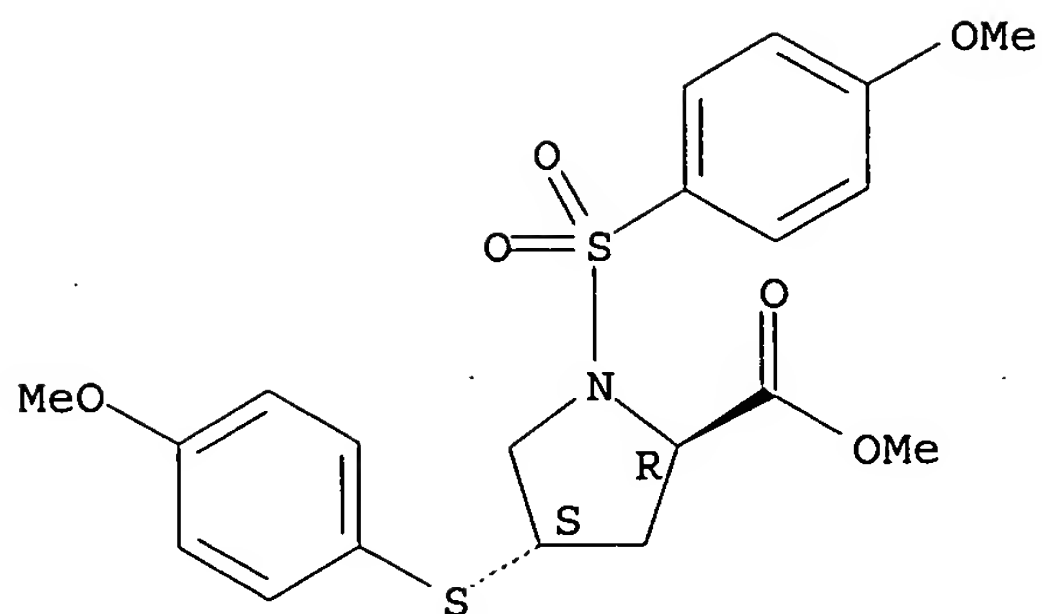
Relative stereochemistry.



RN 204072-41-3 HCAPLUS

CN D-Proline, 4-ethyl-4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

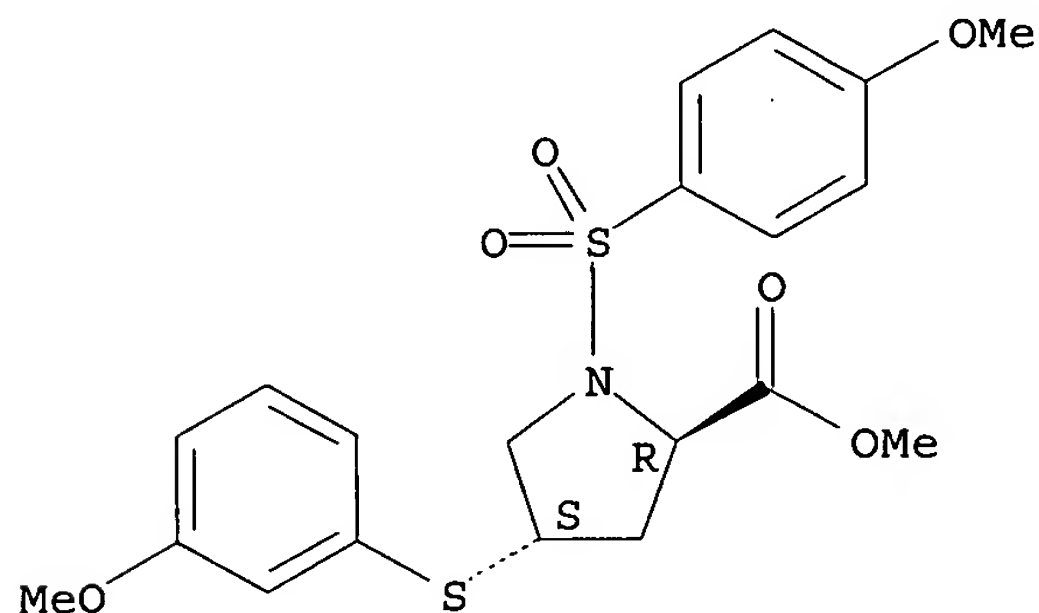
Absolute stereochemistry.



RN 204072-34-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(3-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

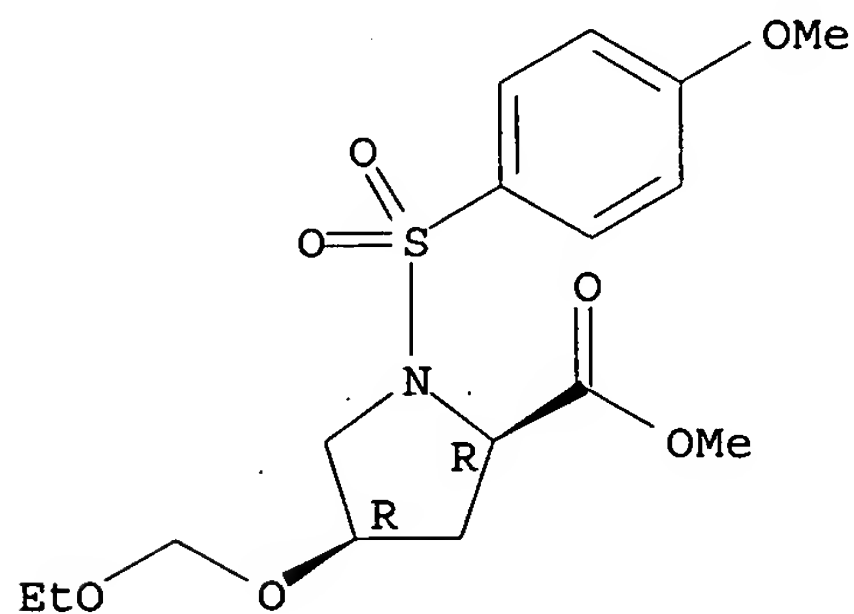
Absolute stereochemistry.



RN 204072-36-6 HCAPLUS

CN D-Proline, 4-(ethoxymethoxy)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

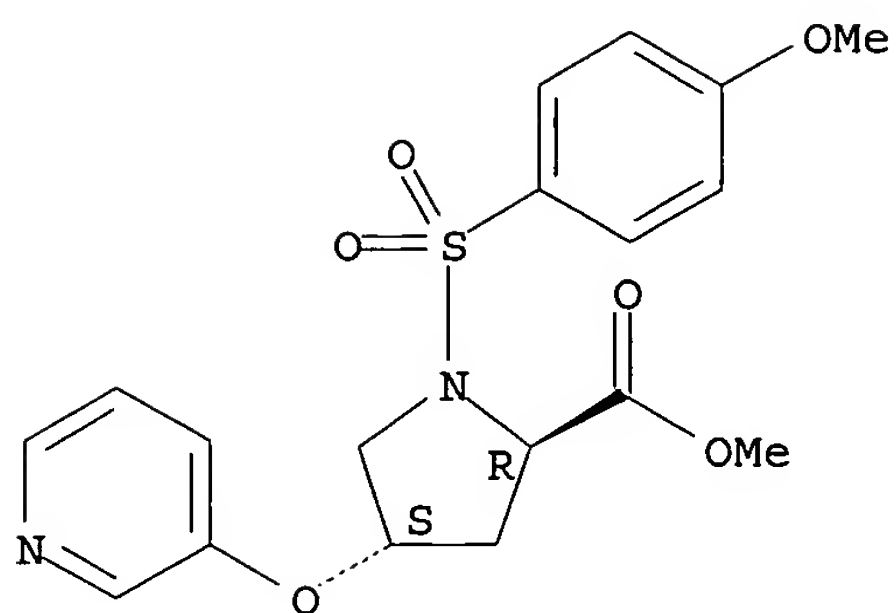
Absolute stereochemistry.



RN 204072-37-7 HCAPLUS

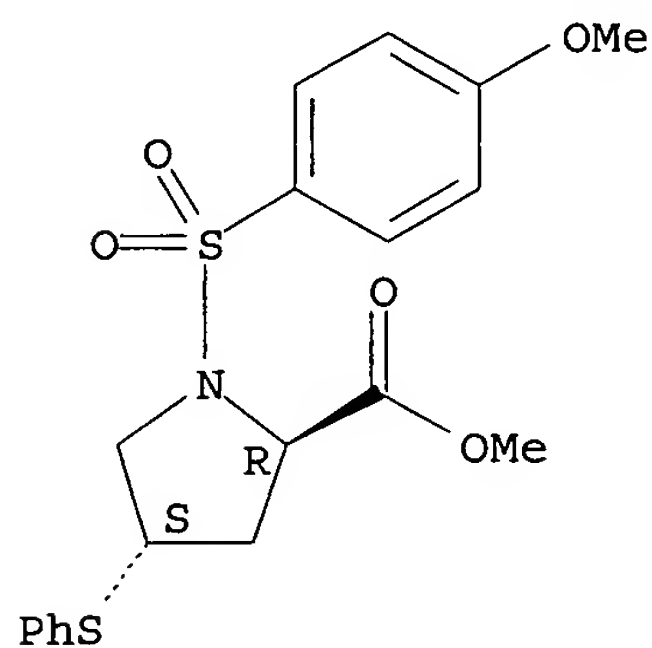
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(phenylmethoxy)methoxy]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



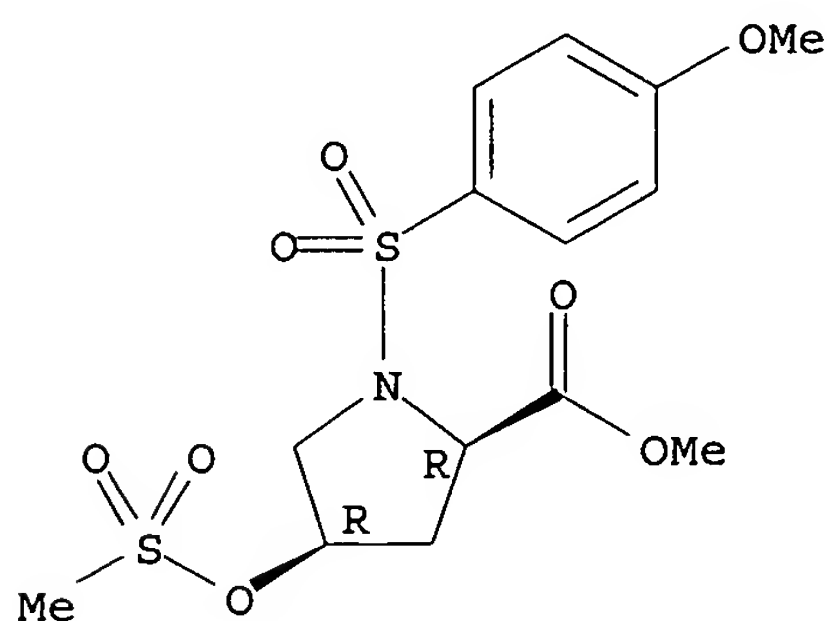
RN 204072-30-0 HCAPLUS  
 CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(phenylthio)-, methyl ester,  
 (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



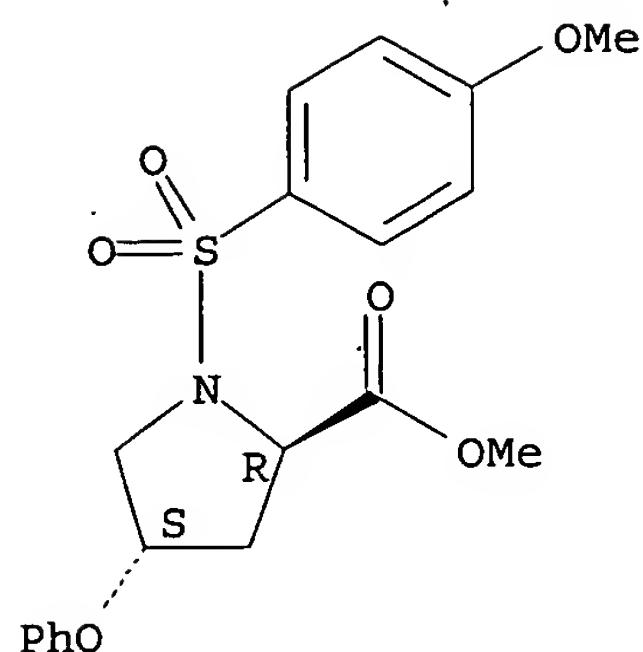
RN 204072-31-1 HCAPLUS  
 CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)oxy]-, methyl  
 ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



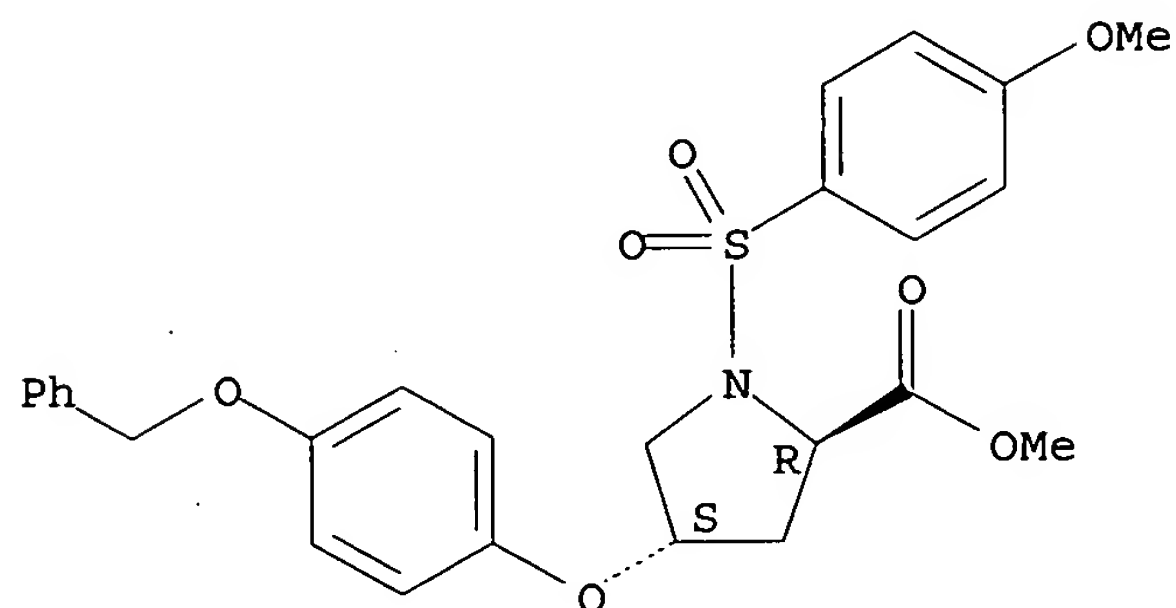
RN 204072-32-2 HCAPLUS  
 CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(4-methoxyphenyl)thio]-,  
 methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



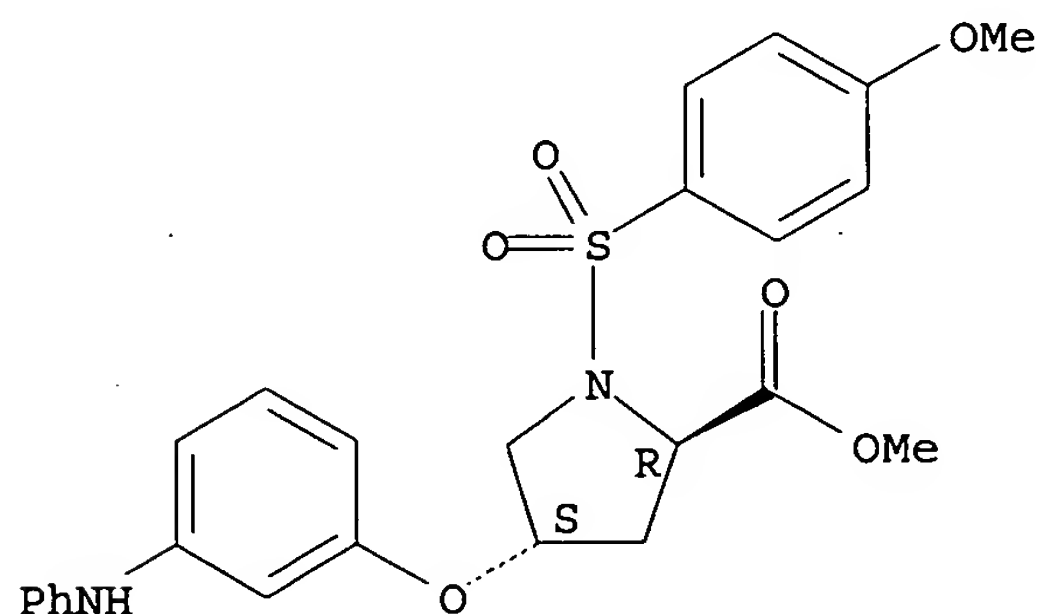
RN 204072-27-5 HCAPLUS  
 CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[4-(phenylmethoxy)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-28-6 HCAPLUS  
 CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(phenylamino)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



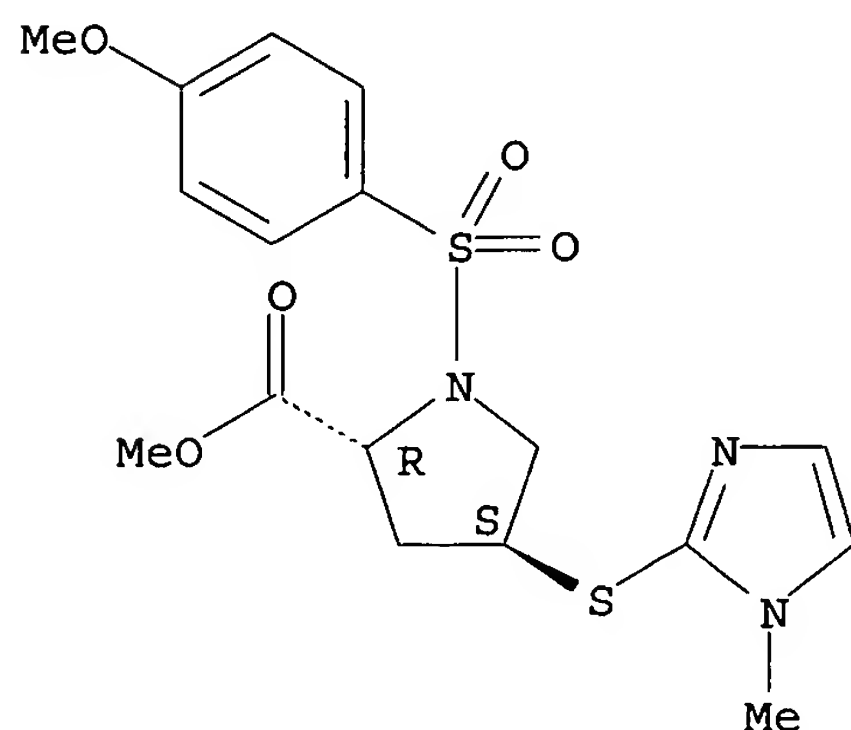
RN 204072-29-7 HCAPLUS  
 CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(3-pyridinyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-24-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-methyl-1H-imidazol-2-yl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

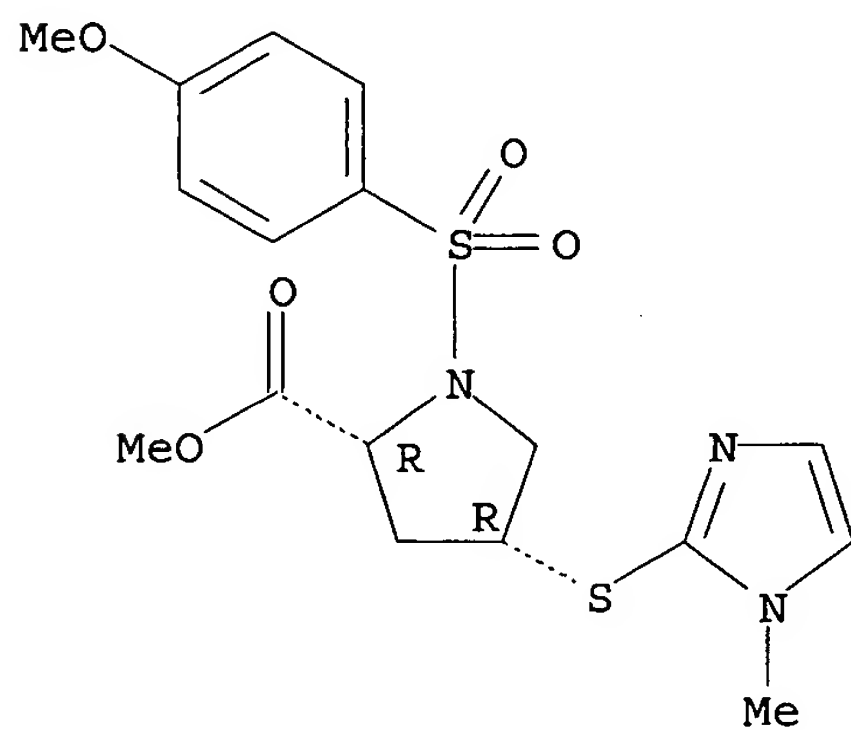
Absolute stereochemistry.



RN 204072-25-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-methyl-1H-imidazol-2-yl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

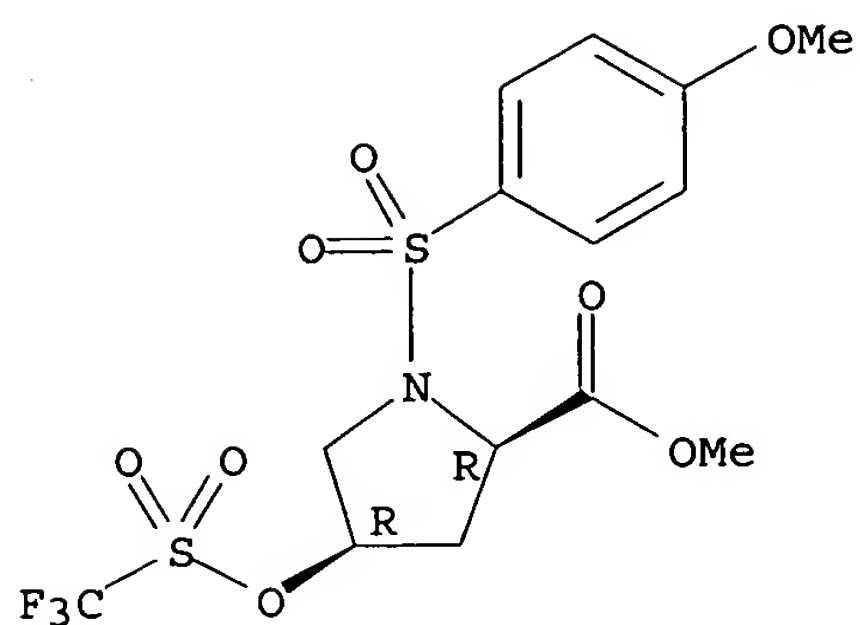
Absolute stereochemistry.



RN 204072-26-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-phenoxy-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

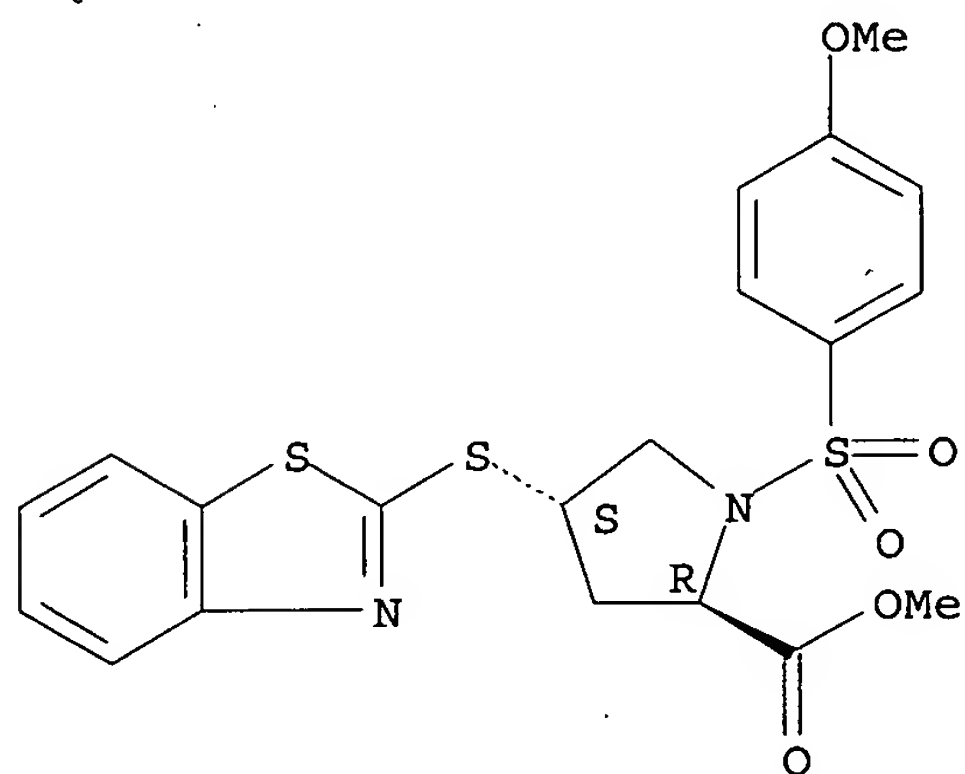
Absolute stereochemistry.



RN 204072-21-9 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

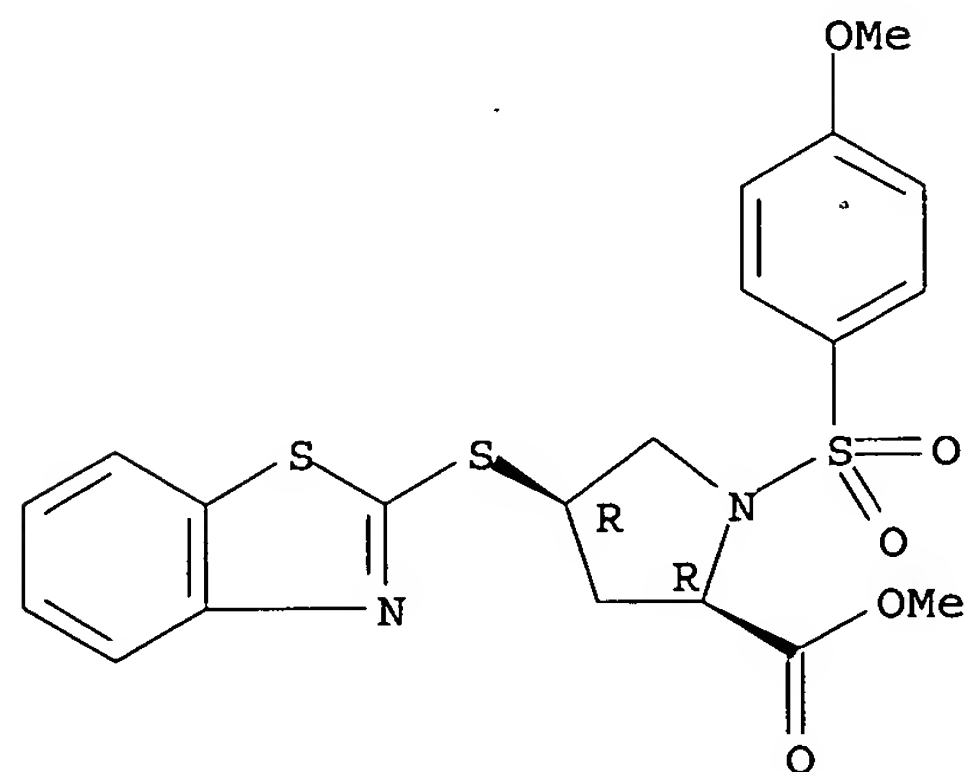
Absolute stereochemistry.

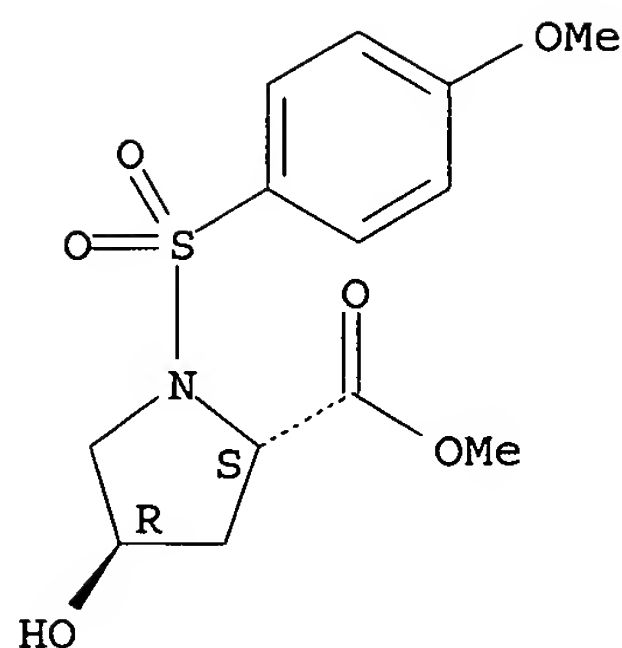


RN 204072-23-1 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

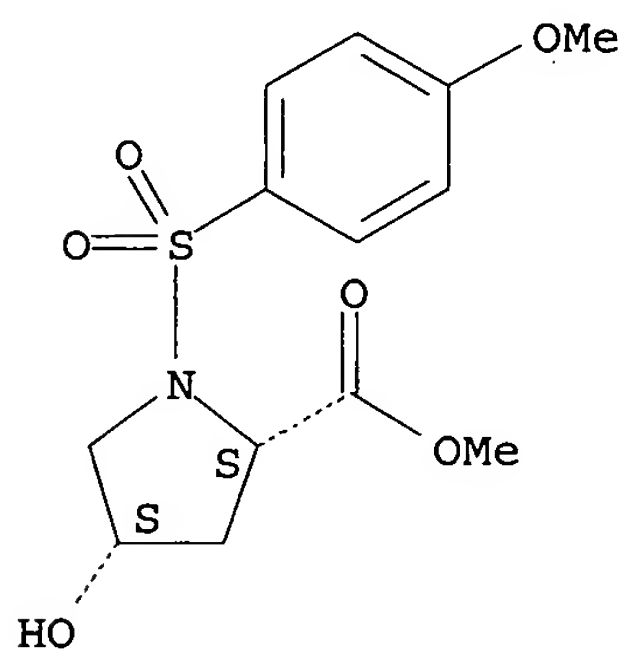




RN 204072-17-3 HCAPLUS

CN L-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

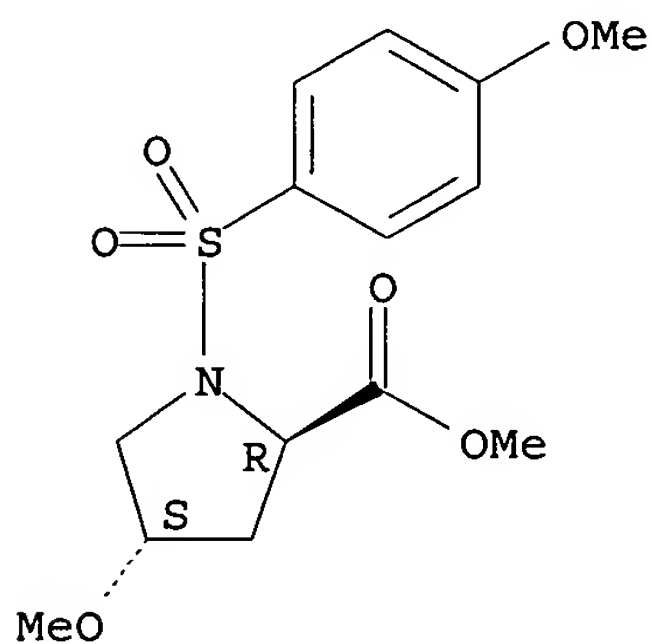
Absolute stereochemistry.



RN 204072-19-5 HCAPLUS

CN D-Proline, 4-methoxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

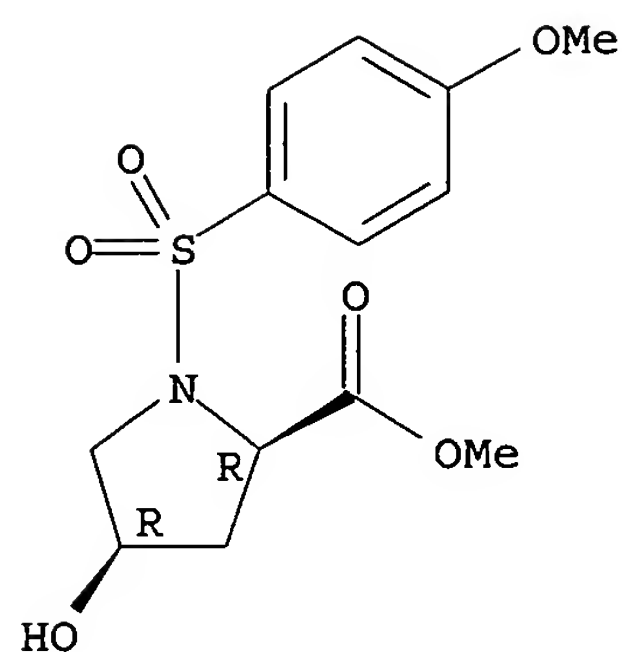


RN 204072-20-8 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[[(trifluoromethyl)sulfonyl]oxy]-], methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

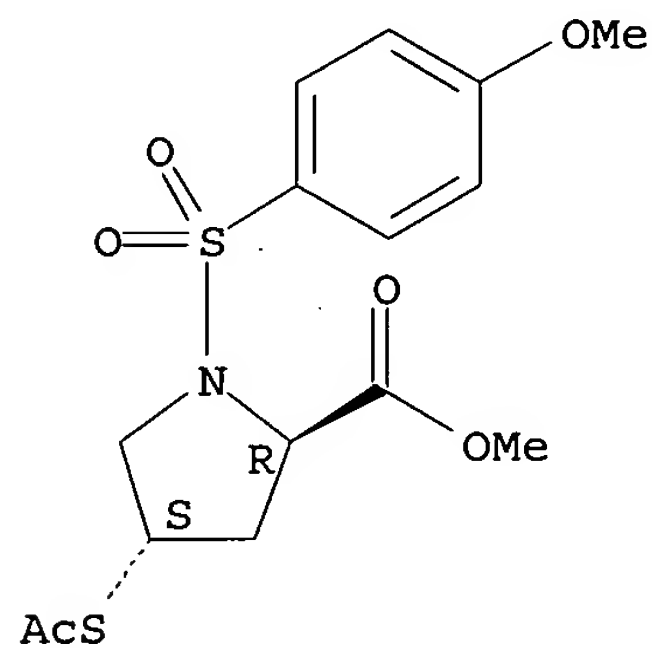




RN 203994-82-5 HCAPLUS

CN D-Proline, 4-(acetylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester,  
(4S)- (9CI) (CA INDEX NAME)

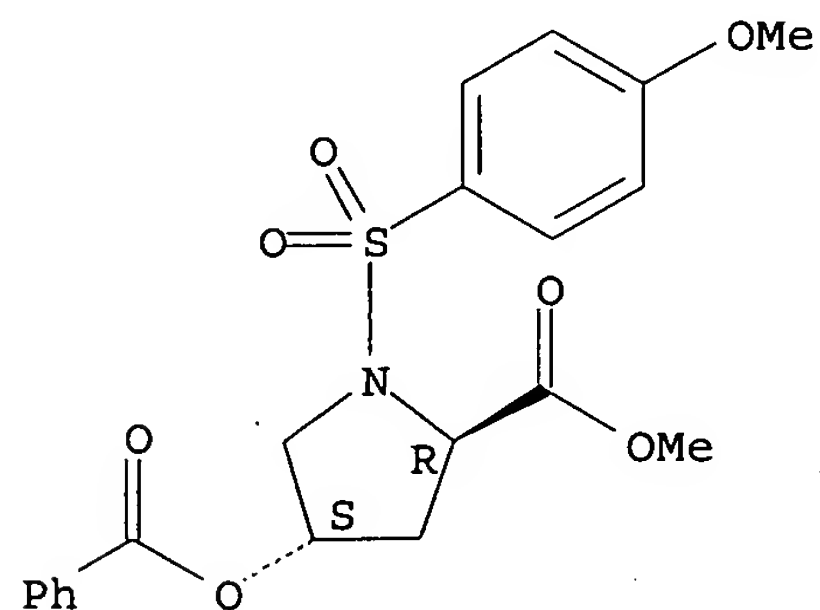
Absolute stereochemistry.



RN 204072-15-1 HCAPLUS

CN D-Proline, 4-(benzoyloxy)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester,  
(4S)- (9CI) (CA INDEX NAME)

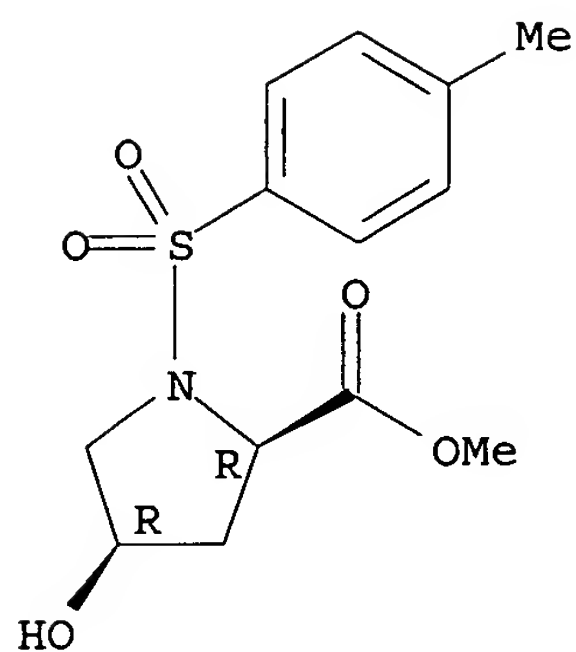
Absolute stereochemistry.



RN 204072-16-2 HCAPLUS

CN L-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)-  
(9CI) (CA INDEX NAME)

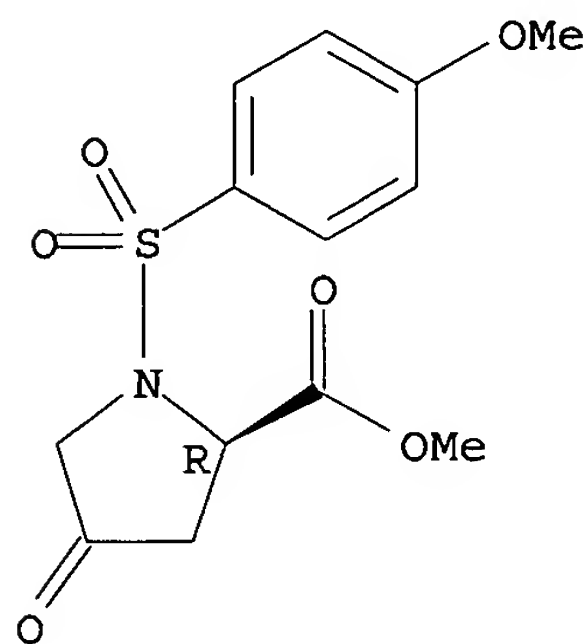
Absolute stereochemistry.



RN 203934-42-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

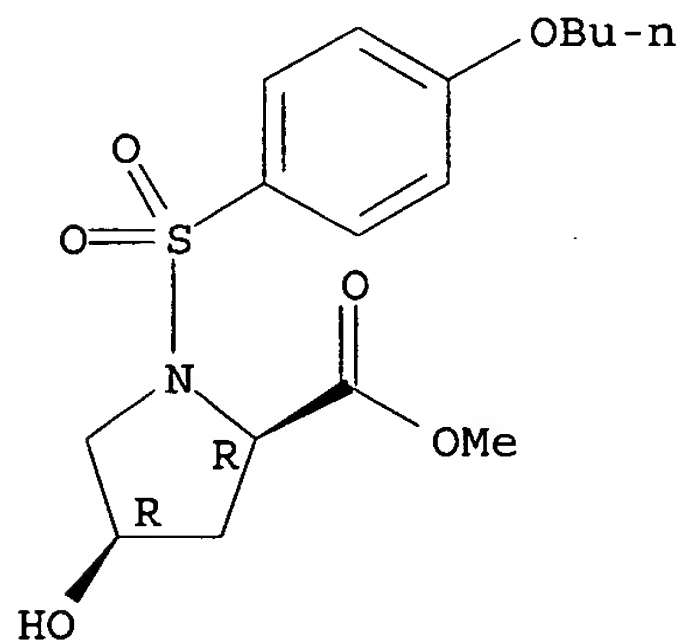
Absolute stereochemistry.



RN 203934-63-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 203994-80-3 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[[(2R)-1-oxo-2-benzyloxypropyl]aminolpyrrolidine 204072-83-3P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[[(2R)-1-oxo-2-benzyloxy-3-phenylpropyl]aminolpyrrolidine 204072-84-4P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-benzyloxypropyl]propylaminolpyrrolidine 204072-85-5P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-hydroxypropyl]propylaminolpyrrolidine 204072-86-6P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-benzyloxy-3-phenylpropyl]propylaminolpyrrolidine 204072-87-7P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-[(2R)-1-oxo-2-hydroxy-3-phenylpropyl]propylaminolpyrrolidine 204072-88-8P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-piperidyl)pyrrolidine 204072-89-9P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-piperidyl)pyrrolidine 204072-90-2P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-morpholinopyrrolidine 204072-91-3P, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-morpholinopyrrolidine 204072-92-4P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-93-5P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204073-01-8P  
 537704-28-2P 537704-31-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-aminopyrrolidine formate 537704-32-8P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[[N-methyl-3-imidazolyl]sulfonyl]aminolpyrrolidine 537704-35-1P  
 537704-63-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-66-8P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-68-0P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-allyl-2,5-dioxoimidazolidin-3-yl)pyrrolidine 537704-72-6P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2,4-dioxo-5,5-dimethylimidazolidin-1-yl)pyrrolidine 537704-74-8P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(5S)-5-methyl-2,4-dioxoimidazolidin-1-yl]pyrrolidine 537704-76-0P,  
 N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-methoxycarbonyl-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-78-2P,  
 N-(4-Phenoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted cyclic amines as metalloprotease inhibitors for treating conditions characterized by excess activity of these enzymes)

RN 57850-07-4 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methylphenyl)sulfonyl]-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

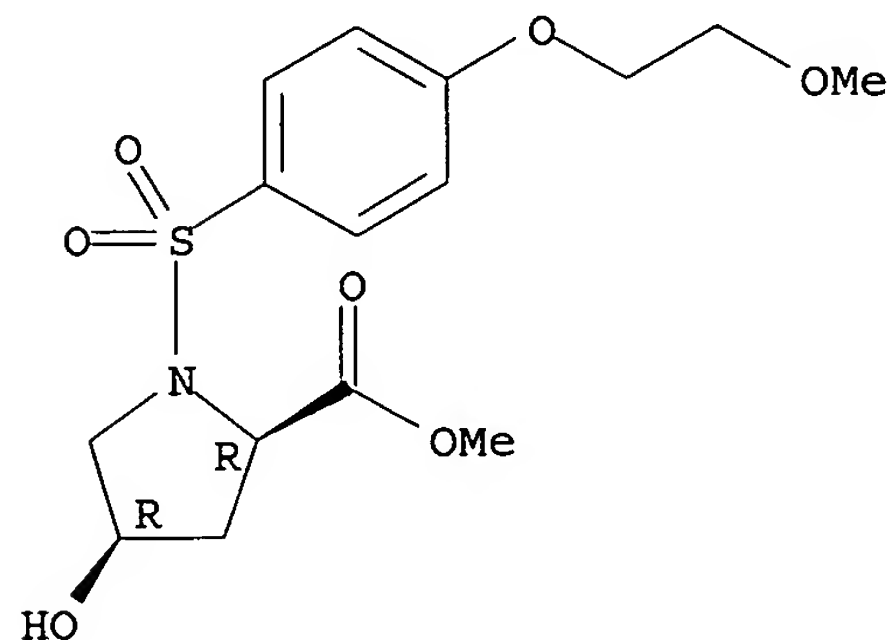
Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-ethoxymethoxypyrrolidine  
**204072-37-7P**, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-  
 (4R)-benzyloxymethoxypyrrolidine **204072-38-8P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[(2-  
 methoxyethoxy)methoxy]pyrrolidine **204072-39-9P**  
**204072-41-3P**, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-  
 (4R)-4-hydroxy-4-ethylpyrrolidine **204072-42-4P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-4-hydroxy-4-  
 phenylpyrrolidine **204072-44-6P**, N-(4-Methoxyphenylsulfonyl)-(2R)-  
 methoxycarbonyl-3,3-dimethyl-4-oxopyrrolidine **204072-45-7P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-3,3-dimethyl-(4R)-  
 hydroxypyrrolidine **204072-46-8P**, N-(3,4-Dimethoxyphenylsulfonyl)-  
 (2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine **204072-47-9P**,  
 N-(2-Nitro-4-methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-  
 hydroxypyrrolidine **204072-49-1P**, N-(4-Butoxyphenylsulfonyl)-(2R)-  
 methoxycarbonyl-(4S)-benzyloxypyrrolidine **204072-50-4P**,  
 N-(4-Bromobenzenesulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine  
**204072-51-5P**, N-(2-Methyl-4-bromobenzenesulfonyl)-(2R)-  
 methoxycarbonyl-(4R)-hydroxypyrrolidine **204072-52-6P**,  
 N-(2,4-Dichlorophenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-  
 hydroxypyrrolidine **204072-55-9P**, N-(4-Phenoxyphenylsulfonyl)-  
 (2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine **204072-56-0P**,  
 N-(4-Isobutyloxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-  
 hydroxypyrrolidine **204072-57-1P**, N-(2-Methyl-4-  
 bromophenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-  
 methoxyphenylthio)pyrrolidine **204072-58-2P**, N-(4-  
 Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-  
 benzothiazolylthio)pyrrolidine **204072-59-3P**,  
 N-(2-Nitro-4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-  
 benzothiazolylthio)pyrrolidine **204072-60-6P**,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-Methoxycarbonyl-(4S)-(4-  
 methoxyphenylthio)pyrrolidine **204072-61-7P**, N-(4-  
 Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-pyridyloxy)pyrrolidine  
**204072-62-8P**, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-  
 (4S)-azidopyrrolidine **204072-64-0P**, N-(4-Butoxyphenylsulfonyl)-  
 (2R)-methoxycarbonyl-(4R)-(methylsulfonyl)pyrrolidine  
**204072-65-1P**, N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-  
 azidopyrrolidine **204072-66-2P**, N-(4-Butoxyphenylsulfonyl)-(2R)-  
 methoxycarbonyl-(4S)-aminopyrrolidine **204072-67-3P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-  
 propylaminopyrrolidine **204072-68-4P**, N-(4-Methoxyphenylsulfonyl)-  
 (2R)-methoxycarbonyl-(4S)-n-hexylaminopyrrolidine **204072-69-5P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(2-  
 phenylethylamino)pyrrolidine **204072-70-8P**, N-(4-  
 Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(N-butyl-N-  
 hexylamino)pyrrolidine **204072-71-9P** **204072-72-0P**,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-  
 [(methanesulfonyl)amino]pyrrolidine **204072-74-2P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(3-  
 pyridylmethyl)amino]pyrrolidine **204072-75-3P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-(3-pyridylmethyl)-  
 N-(methanesulfonyl)amino]pyrrolidine **204072-76-4P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N,N-  
 bis(methanesulfonyl)amino]pyrrolidine **204072-77-5P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-  
 (methanesulfonyl)propylamino]pyrrolidine **204072-78-6P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[(4-  
 methoxyphenylsulfonyl)amino]pyrrolidine **204072-79-7P**,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(1-  
 oxohexyl)aminopyrrolidine **204072-81-1P** **204072-82-2P**,

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (intermediate; preparation of substituted cyclic amines as metalloprotease inhibitors for treating conditions characterized by excess activity of these enzymes)

RN 204072-54-8 HCAPLUS

CN D-Proline, 4-hydroxy-1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-, methyl ester, (4R) - (9CI) (CA INDEX NAME)

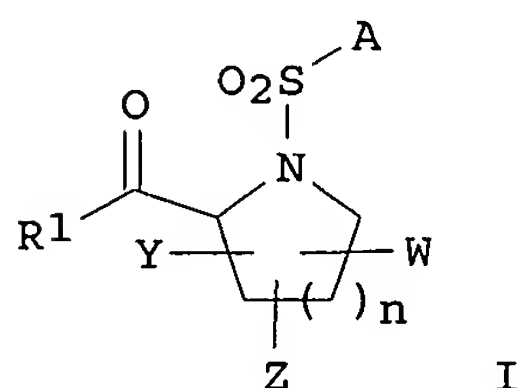
Absolute stereochemistry.



IT 57850-07-4P, N-(4-Methylphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 203934-42-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-4-oxopyrrolidine 203934-63-8P  
 203994-80-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine 203994-82-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-acetylthiopyrrolidine 204072-15-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-benzoyloxypyrrolidine 204072-16-2P, N-(4-Methoxyphenylsulfonyl)-(2S)-methoxycarbonyl-(4R)-hydroxypyrrolidine 204072-17-3P, N-(4-Methoxyphenylsulfonyl)-(2S)-methoxycarbonyl-(4S)-hydroxypyrrolidine 204072-19-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-methoxypyrrolidine 204072-20-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-(trifluoromethanesulfonyloxy)pyrrolidine 204072-21-9P  
 204072-23-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[(benzothiazol-2-yl)thio]pyrrolidine 204072-24-2P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-[N-methyl-2-imidazolylthio]pyrrolidine 204072-25-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-[N-methyl-2-imidazolylthio]pyrrolidine 204072-26-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-phenoxypyrrolidine 204072-27-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(4-benzyloxyphenoxy)pyrrolidine 204072-28-6P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-phenylaminophenoxy)pyrrolidine 204072-29-7P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-pyridinyloxy)pyrrolidine 204072-30-0P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-phenylthiopyrrolidine 204072-31-1P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4R)-(methanesulfonyloxy)pyrrolidine 204072-32-2P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(4-methoxyphenylthio)pyrrolidine 204072-34-4P, N-(4-Methoxyphenylsulfonyl)-(2R)-methoxycarbonyl-(4S)-(3-methoxyphenylthio)pyrrolidine 204072-36-6P, N-(4-

US 2002072517	A1	20020613	US 2001-888759	20010625 <--
US 2003191163	A1	20031009	US 2002-308780	20021203 <--
US 6858628	B2	20050222		
JP 2004115531	A2	20040415	JP 2003-384116	20031113
US 2004138260	A1	20040715	US 2003-730572	20031208
US 2005101567	A1	20050512	US 2004-3594	20041203
PRIORITY APPLN. INFO.:			US 1996-24842P	P 19960828
			US 1997-918317	A2 19970826
			US 2001-888675	A2 20010625
			US 2001-888759	A2 20010625
			JP 1998-511715	A3 19970822
			US 2002-186531	A2 20020701
			US 2002-308780	A3 20021203

OTHER SOURCE(S): MARPAT 139:22213  
GI



AB The invention provides compds. having a structure according to formula (I) [wherein A = each (un)substituted alkyl, heteroalkyl, aryl, heteroaryl; R1 = NHOR2 (where R2 = hydrogen or alkyl); W = H, lower alkyl, or an alkylene bridge that forms a ring in addition to the ring depicted in the formula; Y = HO, SR3, SOR4, SO2R8, alkoxy, (un)substituted NH2; R4 = alkyl, aryl, heteroaryl; R8 = alkyl, aryl, heteroaryl, heteroalkyl, amino, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino; Z = H, HO, alkyl, or an alkylene or heteroalkylene bridge that forms a ring in addition to the ring depicted in the formula; n = 1; provisos given] or pharmaceutically acceptable salts, or biohydrolyzable amides, esters, or imides thereof. These compds. are useful as **inhibitors** of metalloproteases, in particular zinc metalloprotease, and effective in treating conditions characterized by excess activity of these **enzymes**, e.g. degenerative diseases such as arthritis and multiple sclerosis and inflammation (no data). Thus, cis-Hydroxy-D-proline (50 g, 0.38 mol) was dissolved in water:dioxane (1:1, 300 mL) with Et3N (135 mL, 0.96 mol), treated with 4-Methoxyphenylsulfonyl chloride (87 g, 0.42 mol) along with 2,6-dimethylaminopyridine (4.6 g, 0.038 mol), stirred for 14 h at room temperature, concentrated, and diluted with EtOAc to give, after workup, N-(4-Methoxyphenylsulfonyl)-(4R)-hydroxypyrrolidine-(2R)-carboxylic acid. This intermediate was dissolved in MeOH (500 mL), treated dropwise with 50 mL SOCl2, stirred for 14 h, evaporated, to dryness, and triturated with CHCl3 to give N-4-Methoxyphenylsulfonyl-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine as a white solid which was sufficiently pure to carry forward without purification. The latter Me ester (361 mg, 1.15 mmol) was taken in 1 mL MeOH, treated with NH2OK (1.45 mL, 0.86 M in methanol), and stirred overnight to give, after workup, N-4-Methoxyphenylsulfonyl-(2R)-N-hydroxycarboxamido-(4S)-hydroxypyrrolidine.

IT **204072-54-8P**, N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-methoxycarbonyl-(4R)-hydroxypyrrolidine



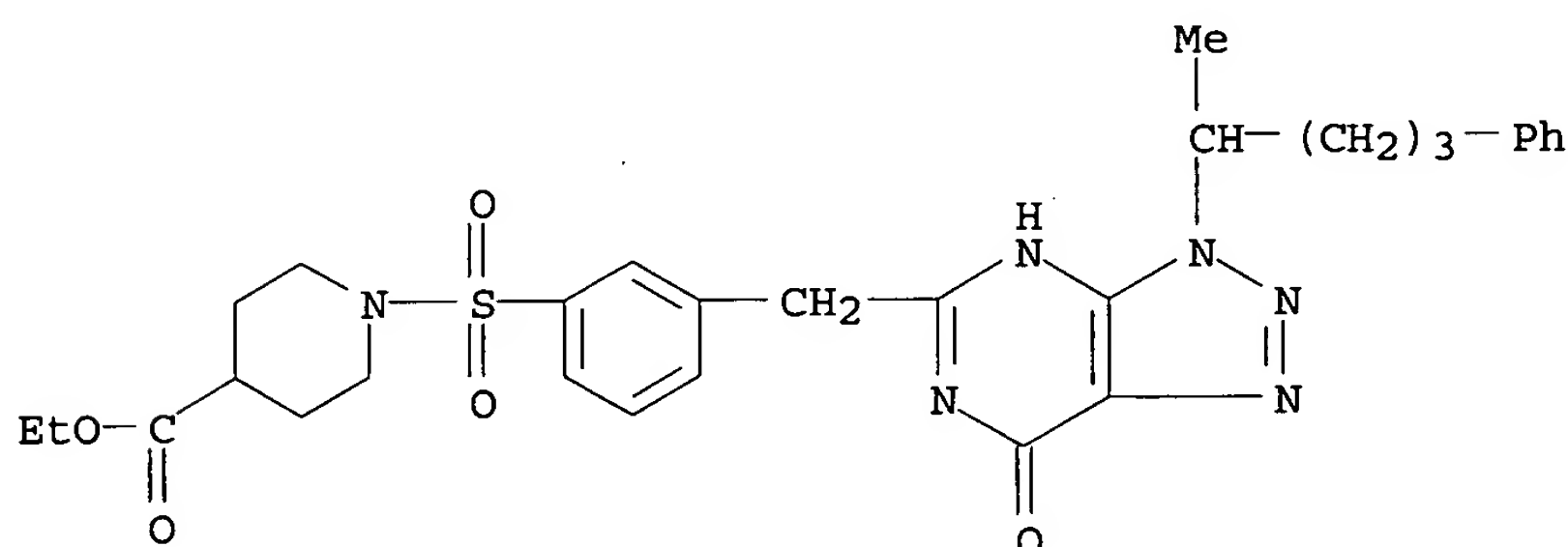
EP 1461022 A2 20040929 EP 2002-796635 20021214  
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 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
 JP 2005513060 T2 20050512 JP 2003-552279 20021214  
 PRIORITY APPLN. INFO.: EP 2001-129951 A 20011217  
 EP 2002-9555 A 20020426  
 EP 2002-23936 A 20021025  
 WO 2002-EP14279 W 20021214

AB The invention discloses the use of PDE5 inhibitors for the treatment of  
 patients having a pulmonary disorder in which in which a pulmonary  
 ventilation-pulmonary perfusion mismatch is present.

IT 259191-82-7  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (phosphodiesterase 5 inhibitors for treatment of pulmonary  
 disease with ventilation-perfusion mismatch)

RN 259191-82-7 HCAPLUS

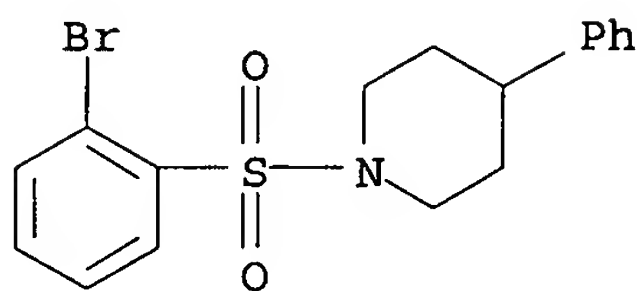
CN 4-Piperidinecarboxylic acid, 1-[[3-[[4,7-dihydro-3-(1-methyl-4-  
 phenylbutyl)-7-oxo-3H-1,2,3-triazolo[4,5-d]pyrimidin-5-  
 yl)methyl]phenyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)



L32 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2003:435318 HCAPLUS  
 DOCUMENT NUMBER: 139:22213  
 TITLE: Preparation of substituted cyclic amines as  
 metalloprotease inhibitors  
 INVENTOR(S): Natchus, Michael George; De, Biswanath; Pikul,  
 Stanislaw; Almstead, Neil Gregory; Bookland, Roger  
 Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan  
 PATENT ASSIGNEE(S): The Procter & Gamble Company, USA  
 SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S.  
 Ser. No. 888,675.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

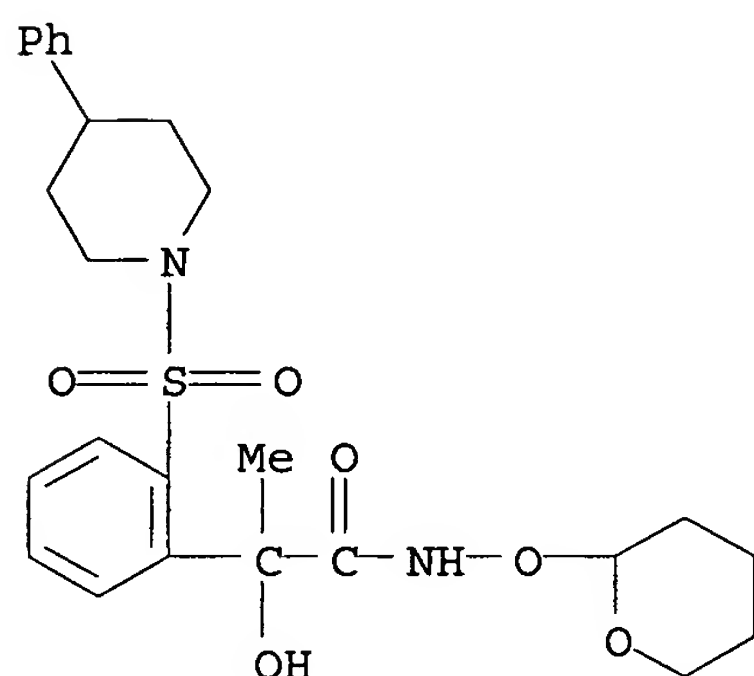
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003105153	A1	20030605	US 2002-186531	20020701 <--
US 6872742	B2	20050329		
US 6417219	B1	20020709	US 1997-918317	19970826 <--
US 2002061877	A1	20020523	US 2001-888675	20010625 <--
US 6569855	B2	20030527		

CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)



RN 308386-08-5 HCAPLUS

CN Benzeneacetamide,  $\alpha$ -hydroxy- $\alpha$ -methyl-2-[(4-phenyl-1-piperidiny]sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:491029 HCAPLUS

DOCUMENT NUMBER: 139:63337

TITLE: Use of selective phosphodiesterase 5 (PDE5) inhibitors in the treatment of pulmonary diseases having a ventilation-perfusion mismatch

INVENTOR(S): Ghofrani, Ardeschir; Grimminger, Friedrich Josef; Schudt, Christian

PATENT ASSIGNEE(S): Altana Pharma AG, Germany

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

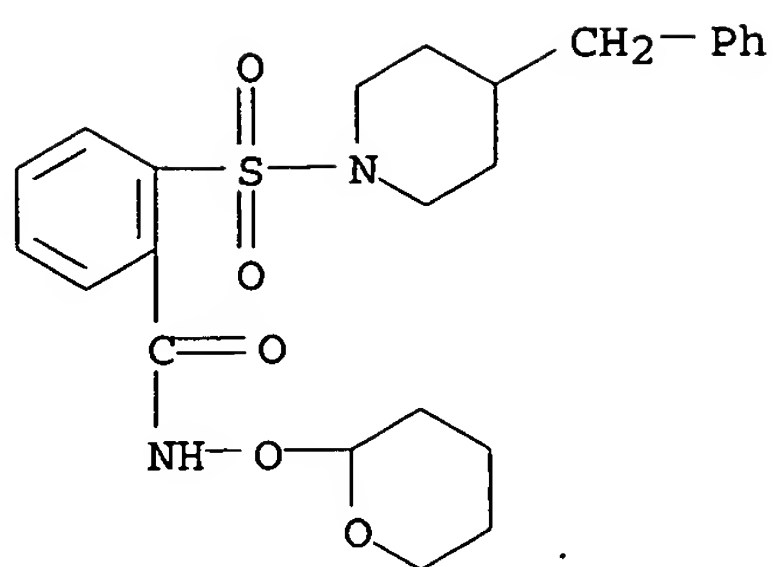
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

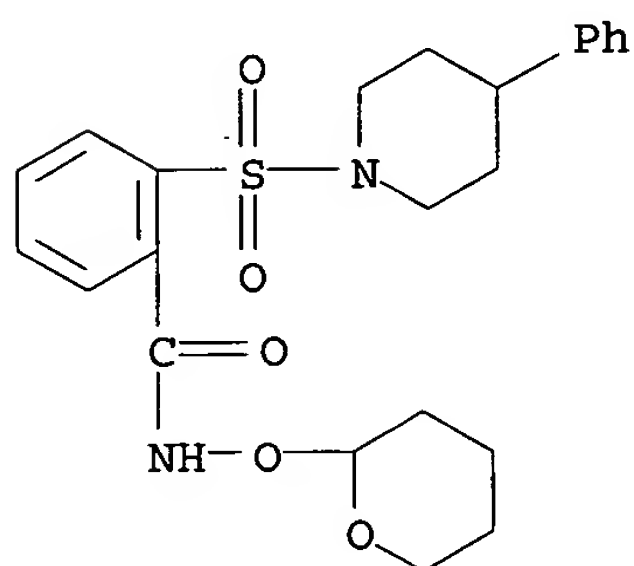
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051346	A2	20030626	WO 2002-EP14279	20021214 <--
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W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				

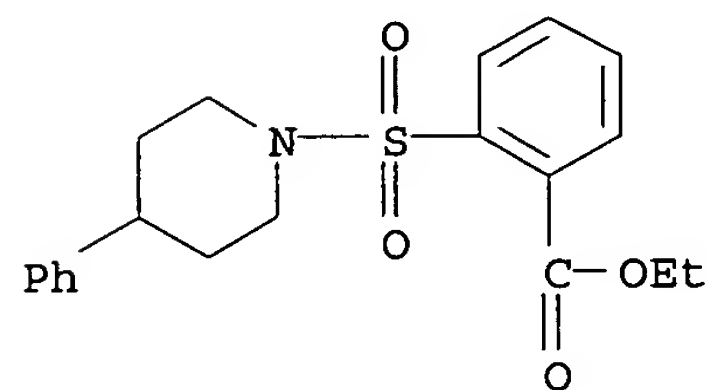




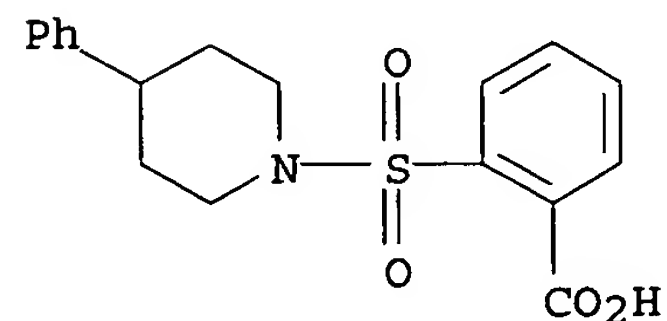
RN 308385-92-4 HCAPLUS  
 CN Benzamide, 2-[(4-phenyl-1-piperidinyl)sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



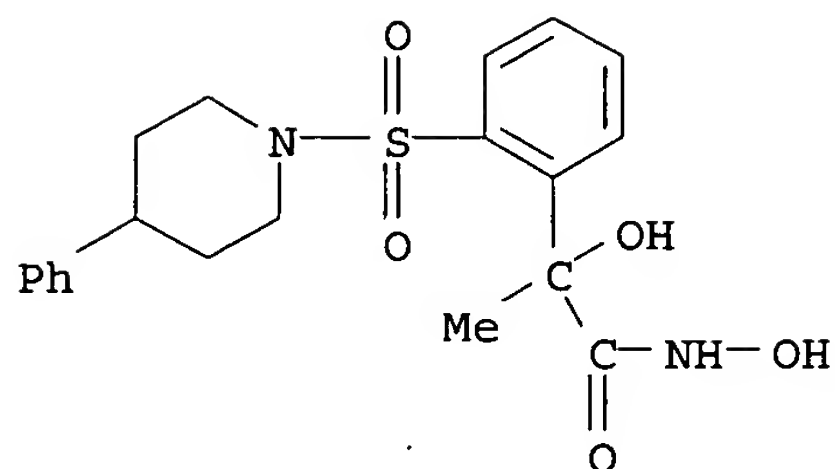
RN 308386-04-1 HCAPLUS  
 CN Benzoic acid, 2-[(4-phenyl-1-piperidinyl)sulfonyl]-, ethyl ester (9CI)  
 (CA INDEX NAME)



RN 308386-05-2 HCAPLUS  
 CN Benzoic acid, 2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 308386-06-3 HCAPLUS



IT 213012-83-0P 213012-84-1P 213012-85-2P

308385-92-4P 308386-04-1P 308386-05-2P

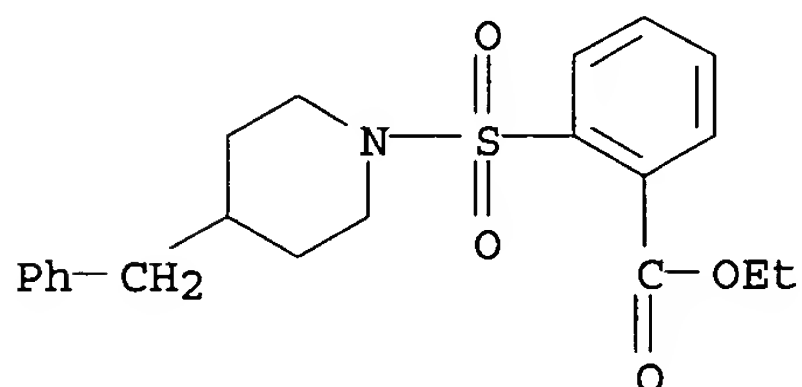
308386-06-3P 308386-08-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as matrix metalloprotease **inhibitors**)

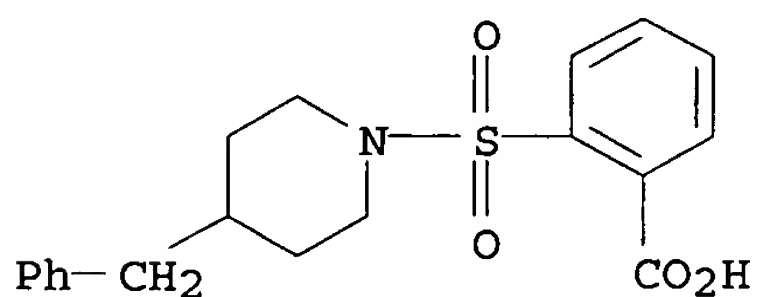
RN 213012-83-0 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 213012-84-1 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 213012-85-2 HCAPLUS

CN Benzamide, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

effective amount to a host having a condition associated with pathol. MMP activity. Thus, thioetherification of 4-phenoxybenzenethiol with 2-fluorobenzaldehyde in the presence of K<sub>2</sub>CO<sub>3</sub> in isopropanol under reflux for 20 h gave 2-(4-phenoxyphenylthio)benzaldehyde which was condensed with tetra-Et dimethylaminomethylenediphosphonate in the presence of NaH in THF at room temperature for 4 h gave to 2-[2-(4-phenoxyphenylthio)phenyl]acetic acid

(II). II was oxidized by H<sub>2</sub>O<sub>2</sub> in acetic acid to 2-[2-(4-phenoxyphenylsulfonyl)phenyl]acetic acid which was condensed with O-tetrahydropyranylhydroxylamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in MeCN followed by treatment with p-toluenesulfonic acid in methanol at room temperature for 2 h to

give N-hydroxy-2-[2-(4-phenoxyphenylsulfonyl)phenyl]acetamide (III). III and N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide showed IC<sub>50</sub> of >10,000 nM against MMP-1, 0.3 and 2.4 nM, resp., against MMP-2, and 2 and 2.7 nM, resp., against MMP-13.

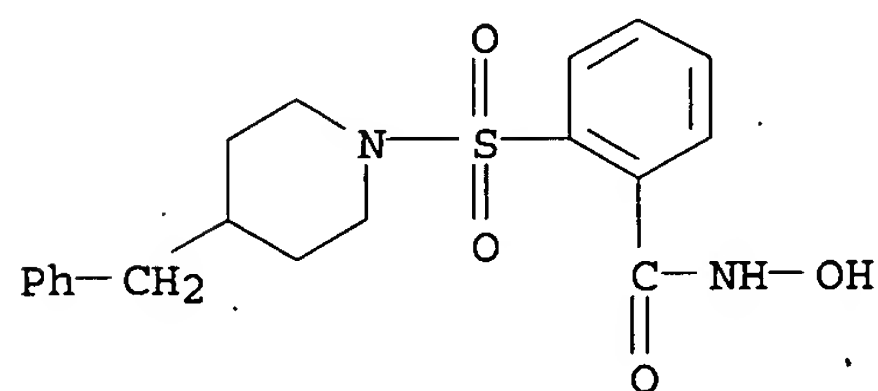
IT 213012-59-0P, N-Hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]benzamide 308385-44-6P, N-Hydroxy-2-[[4-(phenyl)-1-piperidinyl]sulfonyl]benzamide 308385-45-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sulfonyl aryl or heteroaryl hydroxamic acid compds. as matrix metalloprotease inhibitors)

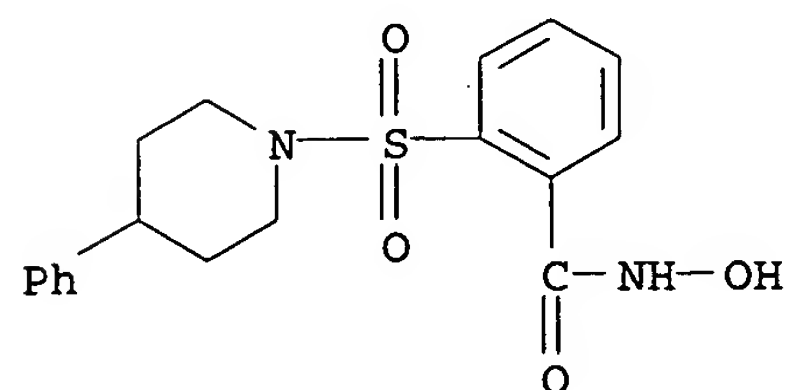
RN 213012-59-0 HCAPLUS

CN Benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-44-6 HCAPLUS

CN Benzamide, N-hydroxy-2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)



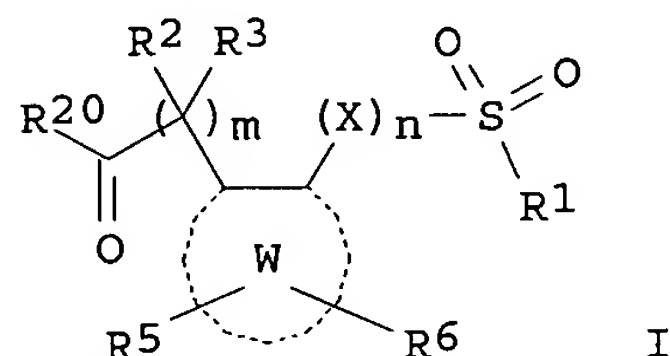
RN 308385-45-7 HCAPLUS

CN Benzeneacetamide, N,α-dihydroxy-α-methyl-2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)

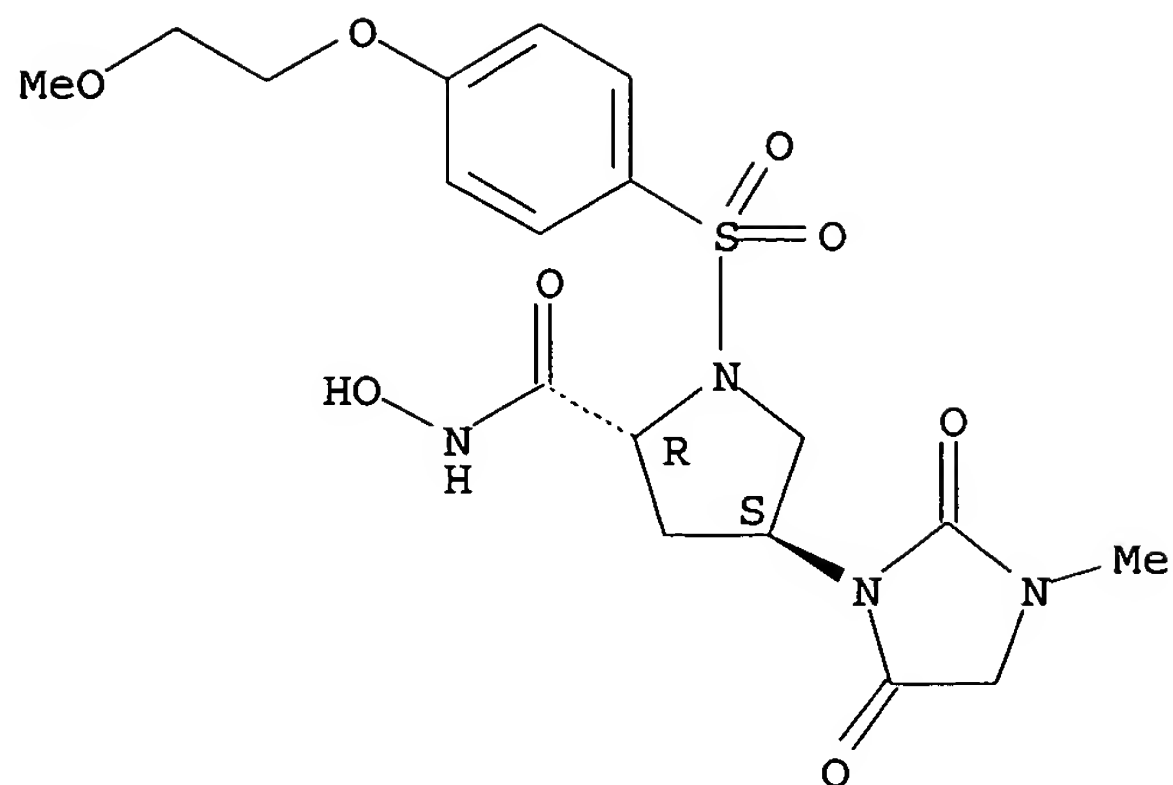
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US 2003191317	A1	20031009	US 2000-728408	20001201 <--
US 6794511	B2	20040921		
WO 9838859	A1	19980911	WO 1998-US4300	19980304 <--
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 2001020021	A1	20010906	US 1999-230209	19990624 <--
US 6380258	B2	20020430		
US 2003073845	A1	20030417	US 2001-909227	20010719 <--
US 6696449	B2	20040224		
US 2005075374	A1	20050407	US 2004-867391	20040614
PRIORITY APPLN. INFO.:			WO 1998-US4300	A1 19980304
			US 1999-310813	B1 19990512
			US 1999-230209	A2 19990624
			US 1997-35182P	P 19970304
			US 2000-569034	A2 20000511
			US 2000-728408	A2 20001201

OTHER SOURCE(S): MARPAT 139:307685

GI



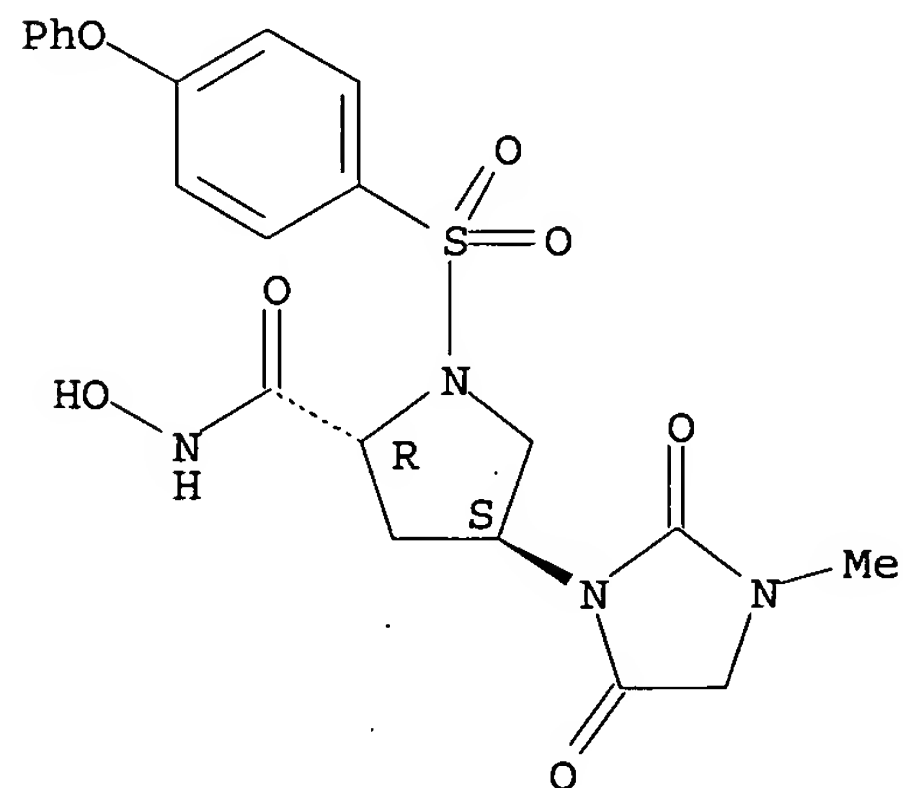
AB The title compds. [I; m, n = 0 or 1 and the sum of m + n is 0 or 1; the ring structure W is a 5- or 6-membered aromatic or heteroarom. ring; X = CH<sub>2</sub> or (un)substituted NH<sub>2</sub>; R<sub>1</sub> = (i) a substituent containing a 5- or 6-membered cyclohydrocarbonyl, heterocyclyl, aryl or heteroaryl radical bonded directly to the depicted SO<sub>2</sub> group or (ii) (un)substituted; R<sub>2</sub>, R<sub>3</sub> = H, alkyl, alkenyl, alkynyl, hydroxyalkyl, O- or S-(un)substituted hydroxyalkyl or mercaptoalkyl, hydroxy, thiol, haloalkyl, N-(un)substituted amino, aminoalkyl, aminoalkanoylaminoalkyl, aminoalkoxy, or aminoalkoxyalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclylthio, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylthio; or CR<sub>2</sub>R<sub>3</sub> together forms an (un)substituted 4- to 8-membered carbocyclic or heterocyclic ring, that is preferably a 5- or 6-membered ring; R<sub>5</sub>, R<sub>6</sub> = H, alkyl, cycloalkyl, acylalkyl, halo, NO<sub>2</sub>, HO, cyano, alkoxy, haloalkyl, haloalkoxy, hydroxyalkyl, N-(un)substituted aminoalkyl or aminoalkoxy, thiol, alkylthio, arylthio, cycloalkylthio, cycloalkoxy, alkoxyalkoxy, perfluoroalkyl, haloalkyl, heterocyclyloxy; or R<sub>5</sub> and R<sub>6</sub> together with the atoms to which they are bonded form a further aliphatic or aromatic carbocyclic or heterocyclic ring having 5- to 7-members; R<sub>20</sub> = each (un)substituted OH, NHOH, or NH<sub>2</sub>] or pharmaceutically acceptable salts thereof are prepared Also disclosed is a treatment process that comprises administering a contemplated sulfonyl aromatic or heteroarom. ring hydroxamic acid compound in a matrix metalloprotease (MMP) **enzyme-inhibiting**



RN 204072-11-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-1-[(4-phenoxyphenyl)sulfonyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L32 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:796371 HCAPLUS

DOCUMENT NUMBER: 139:307685

TITLE: Preparation of sulfonyl aryl or heteroaryl hydroxamic acid compounds as matrix metalloprotease inhibitors  
INVENTOR(S): Bedell, Louis J.; Mcdonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: U.S. Pat. Appl. Publ., 200 pp., Cont.-in-part of U.S. Ser. No. 230,209.

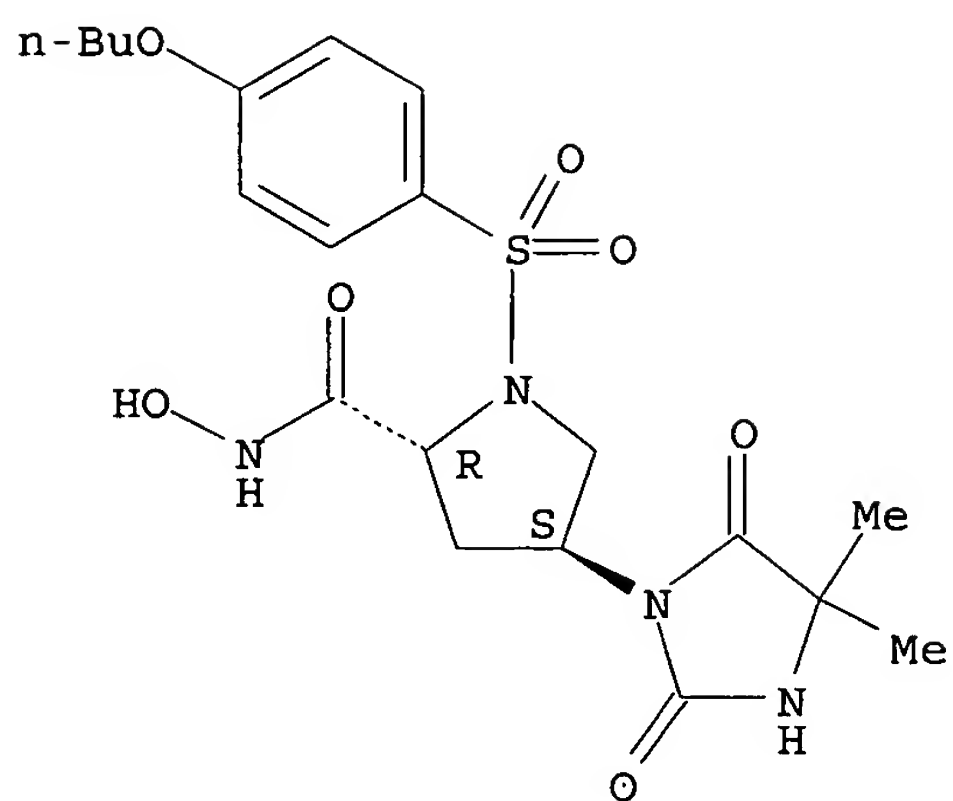
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 10

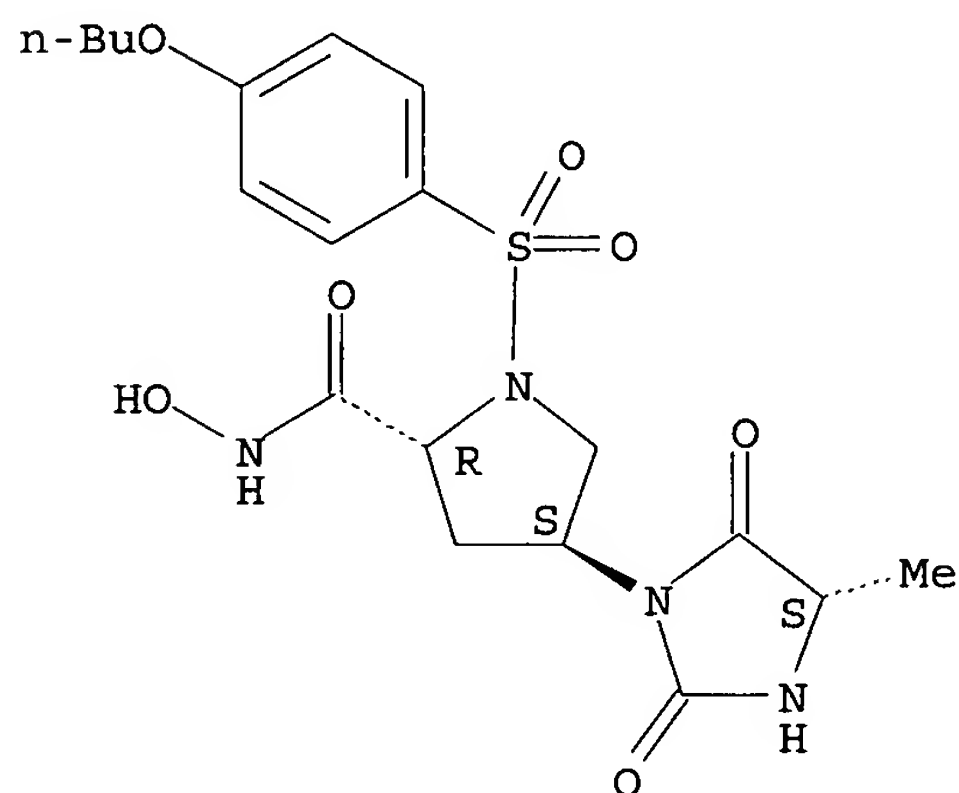
PATENT INFORMATION:



RN 204072-09-3 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-[(4S)-4-methyl-2,5-dioxo-1-imidazolidinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

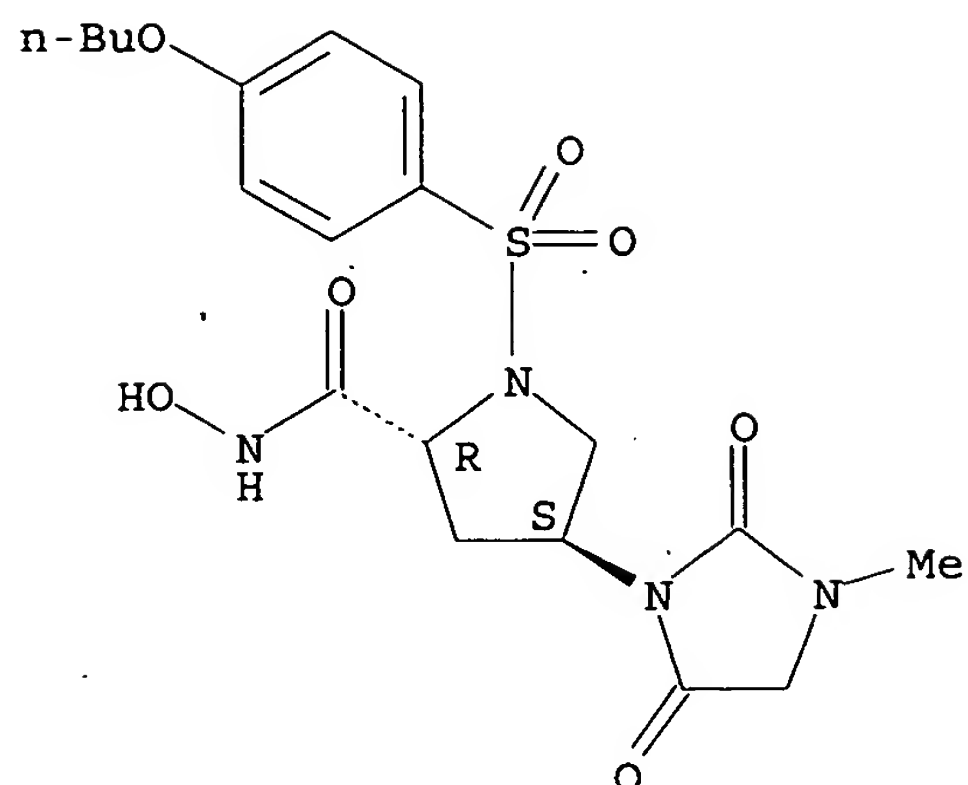
Absolute stereochemistry.



RN 204072-10-6 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

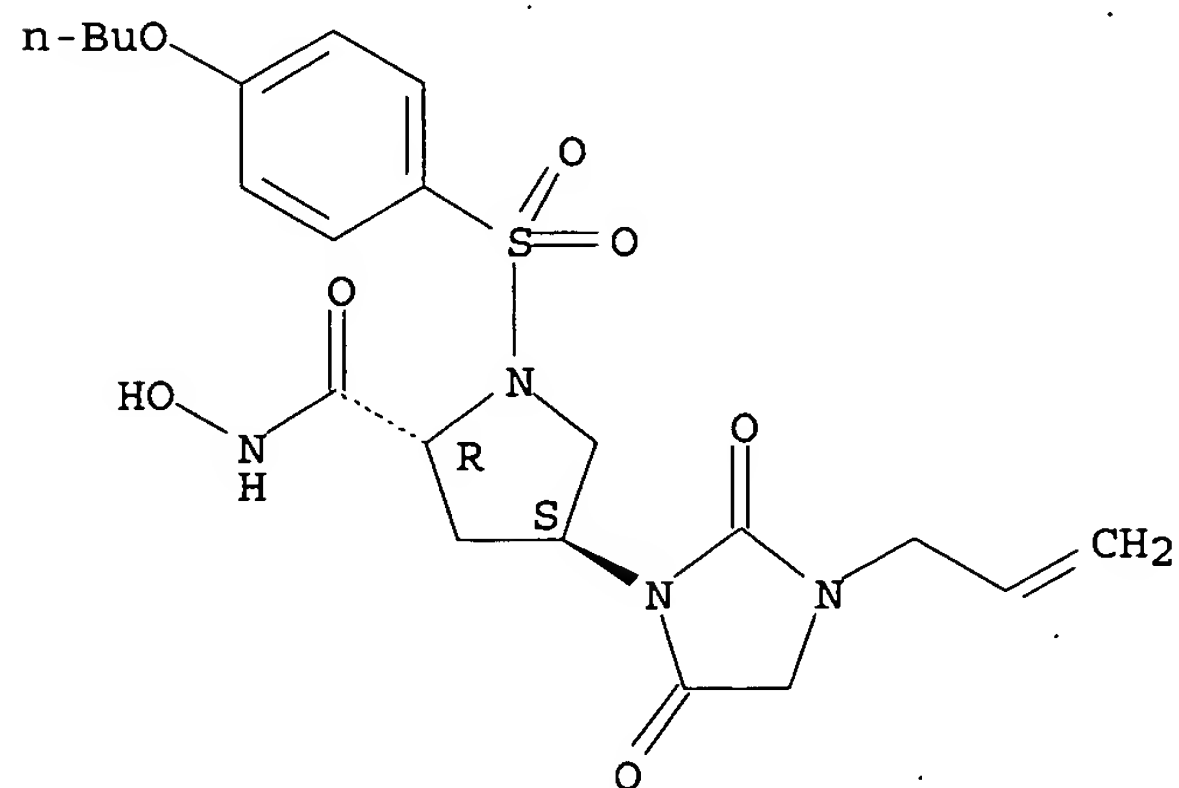
Absolute stereochemistry.



RN 204072-07-1 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-[2,5-dioxo-3-(2-propenyl)-1-imidazolidinyl]-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

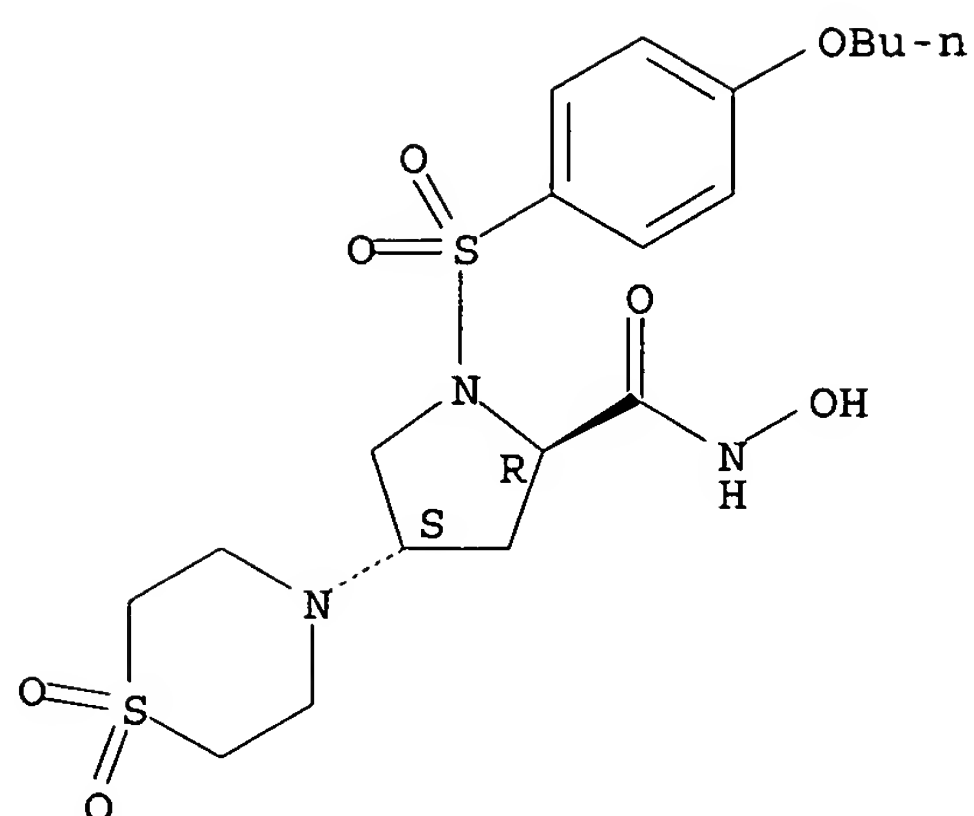
Absolute stereochemistry.



RN 204072-08-2 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-(4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

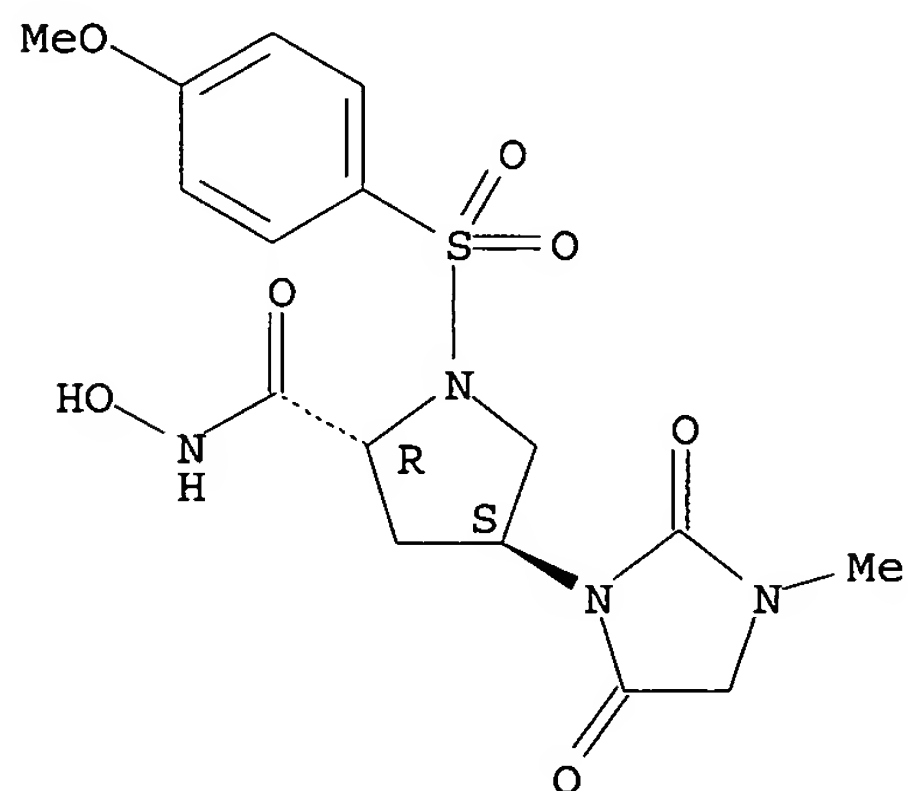
Absolute stereochemistry.



RN 204072-05-9 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

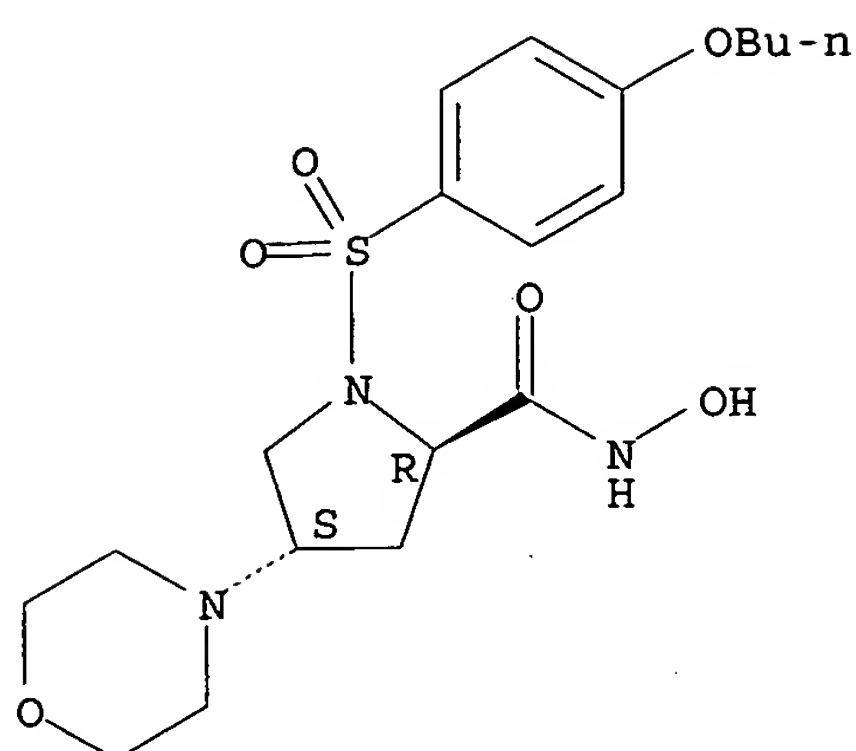


RN 204072-06-0 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

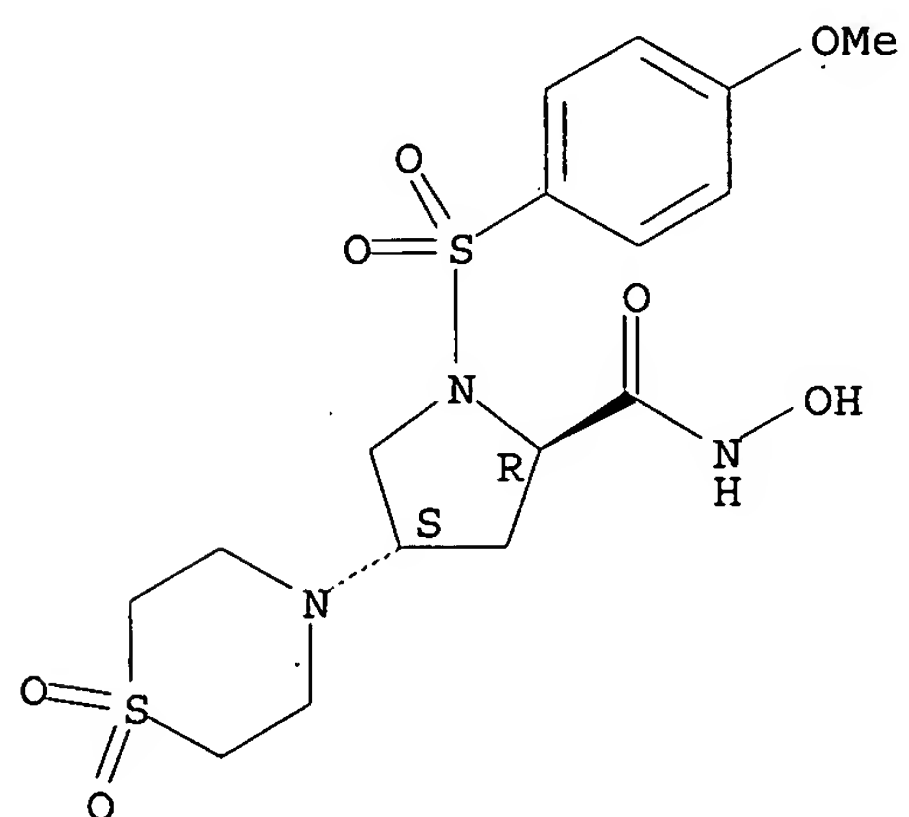




RN 204072-03-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 4-(1,1-dioxido-4-thiomorpholinyl)-N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

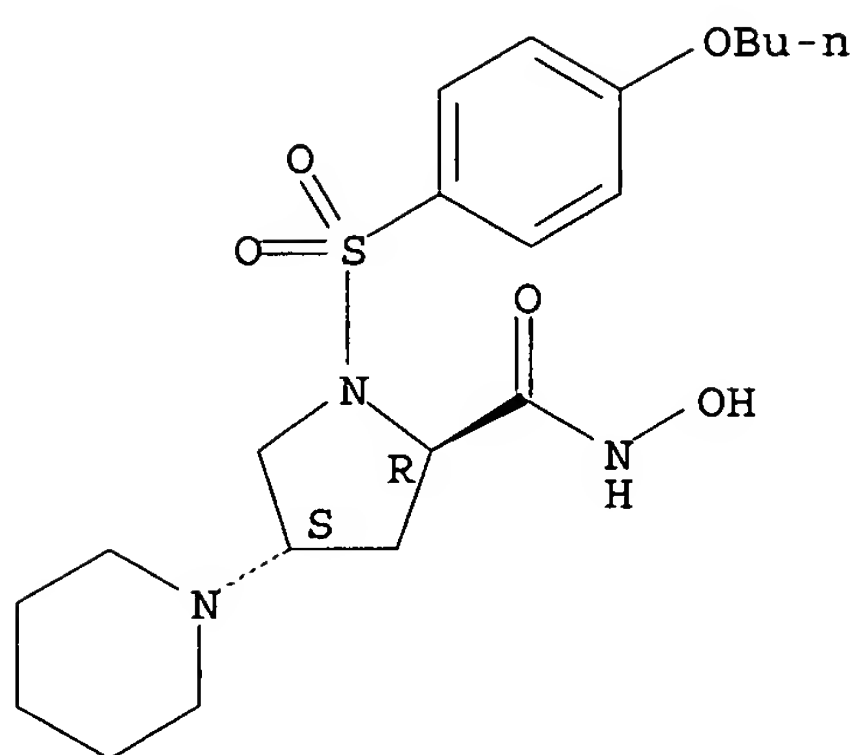
Absolute stereochemistry.



RN 204072-04-8 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-(1,1-dioxido-4-thiomorpholinyl)-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

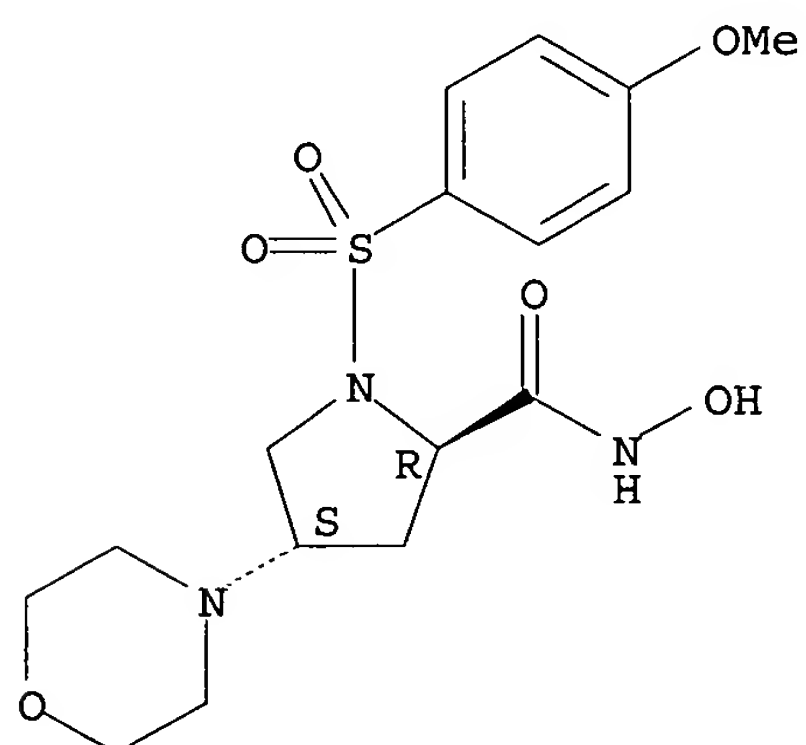
Absolute stereochemistry.



RN 204072-01-5 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

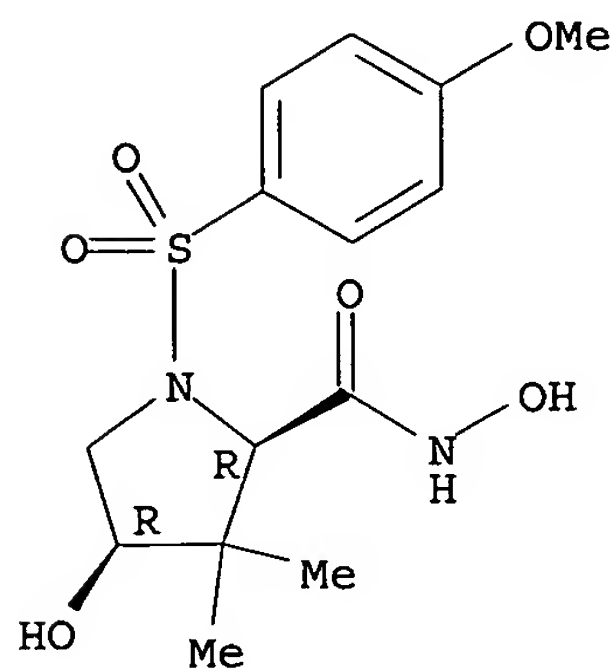


RN 204072-02-6 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(4-morpholinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

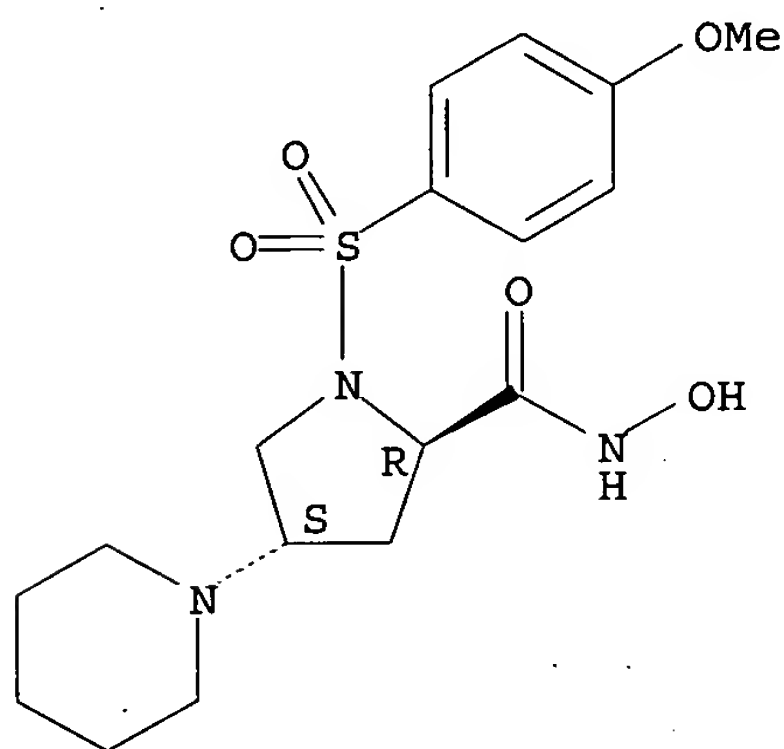
Absolute stereochemistry.



RN 204071-99-8 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

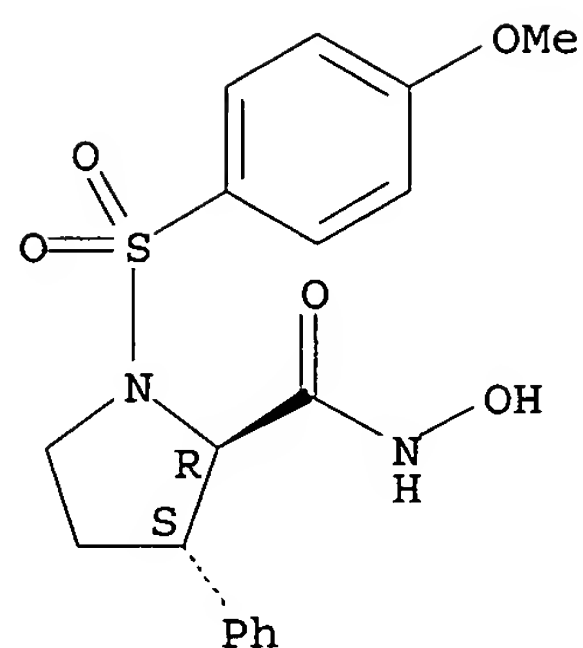
Absolute stereochemistry.



RN 204072-00-4 HCAPLUS

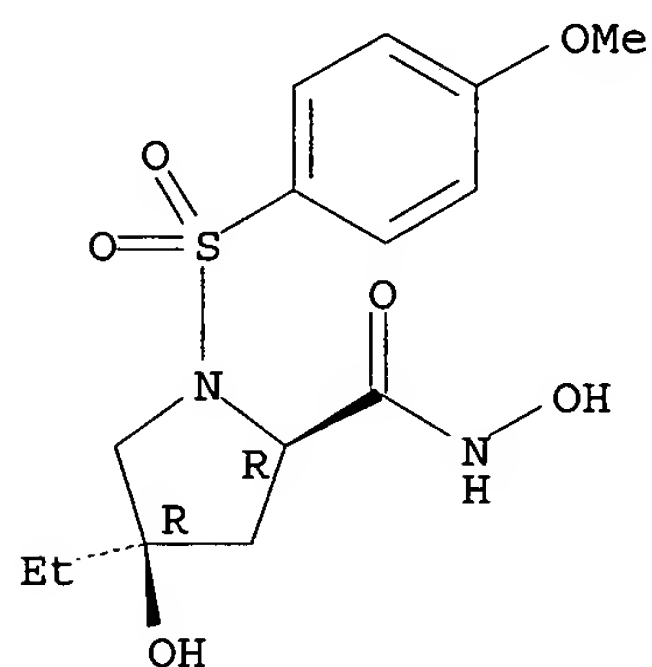
CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(1-piperidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



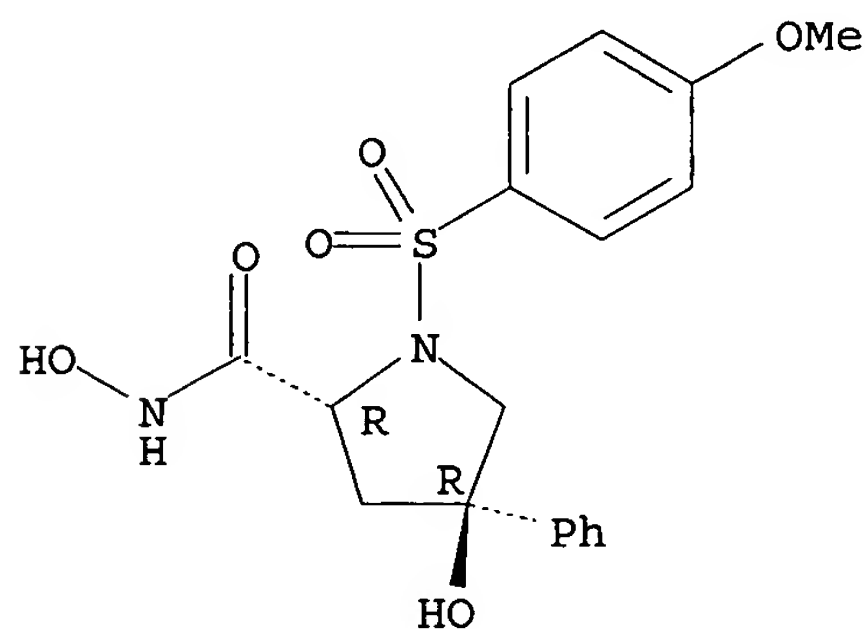
RN 204071-59-0 HCAPLUS  
 CN 2-Pyrrolidinecarboxamide, 4-ethyl-N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204071-60-3 HCAPLUS  
 CN 2-Pyrrolidinecarboxamide, N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-phenyl-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



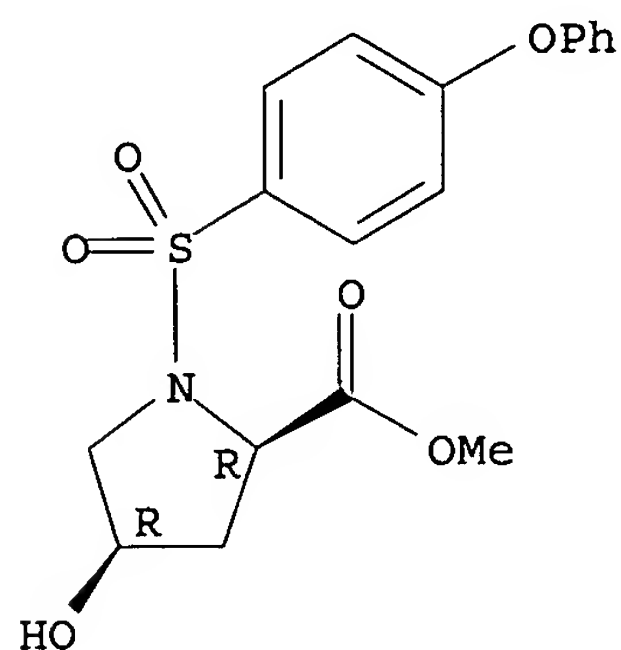
RN 204071-62-5 HCAPLUS  
 CN 2-Pyrrolidinecarboxamide, N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-, (2R,4R)- (9CI) (CA INDEX NAME)

(preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as metalloprotease inhibitors for treatment of restenosis)

RN 204072-55-9 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 204071-58-9P 204071-59-0P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-4-hydroxy-4-ethylpyrrolidine  
 204071-60-3P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-4-hydroxy-4-phenylpyrrolidine  
 204071-62-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-3,3-dimethyl-(4R)-hydroxypyrrolidine  
 204071-99-8P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-piperidyl)pyrrolidine 204072-00-4P,  
 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-piperidyl)pyrrolidine 204072-01-5P, 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(morpholino)pyrrolidine  
 204072-02-6P, 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(morpholino)pyrrolidine 204072-03-7P,  
 1-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-04-8P,  
 1-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-05-9P  
 204072-06-0P 204072-07-1P 204072-08-2P  
 204072-09-3P 204072-10-6P 204072-11-7P

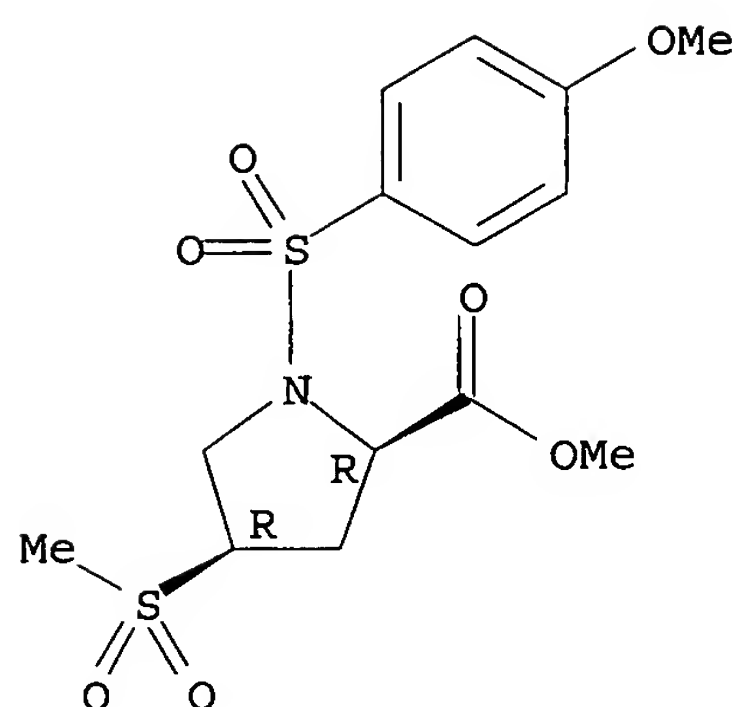
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid as metalloprotease inhibitors for treatment of restenosis)

RN 204071-58-9 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-3-phenyl-, (2R,3S)-rel- (9CI) (CA INDEX NAME)

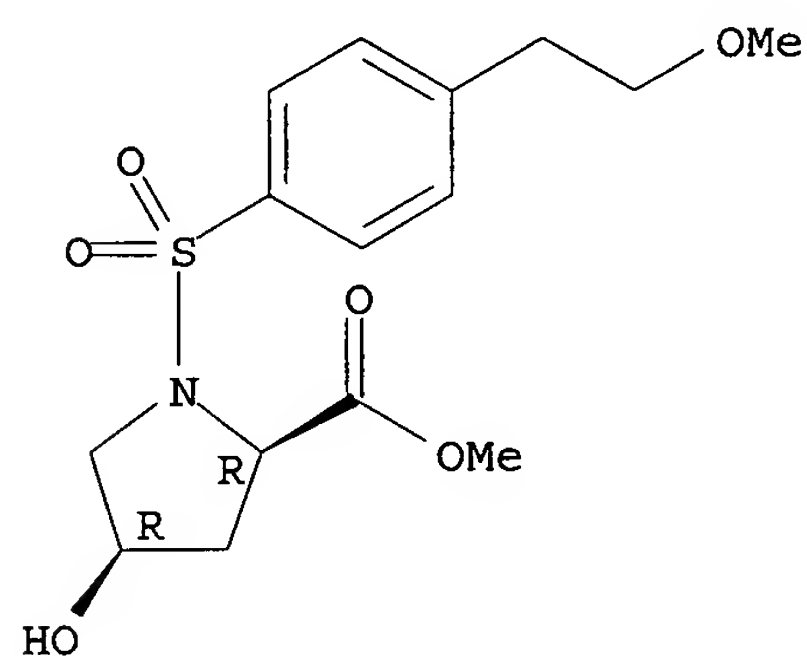
Relative stereochemistry.



RN 722550-49-4 HCAPLUS

CN D-Proline, 4-hydroxy-1-[[4-(2-methoxyethyl)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

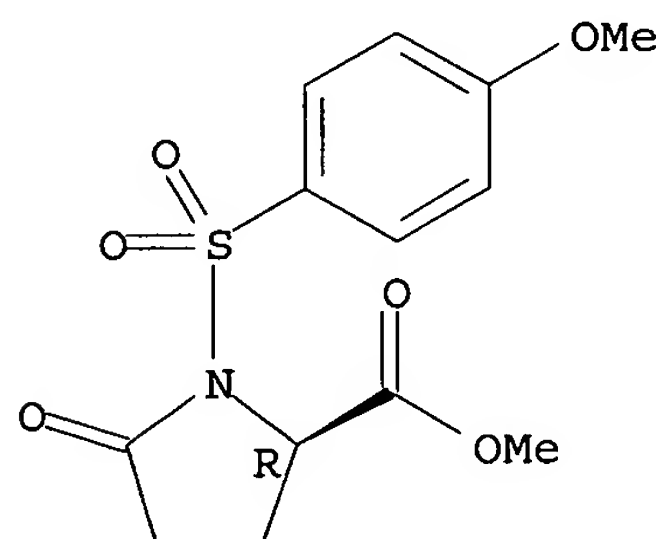
Absolute stereochemistry.



RN 722550-52-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

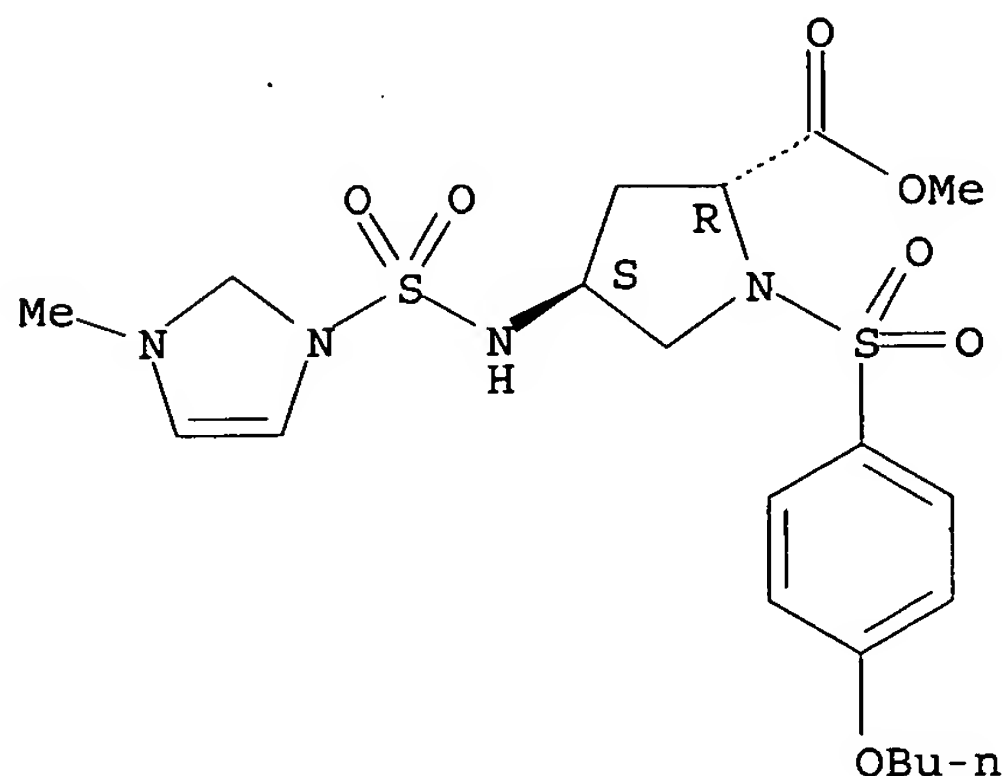


IT 204072-55-9P, 1-(4-Phenoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[[2,3-dihydro-3-methyl-1H-imidazol-1-yl)sulfonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

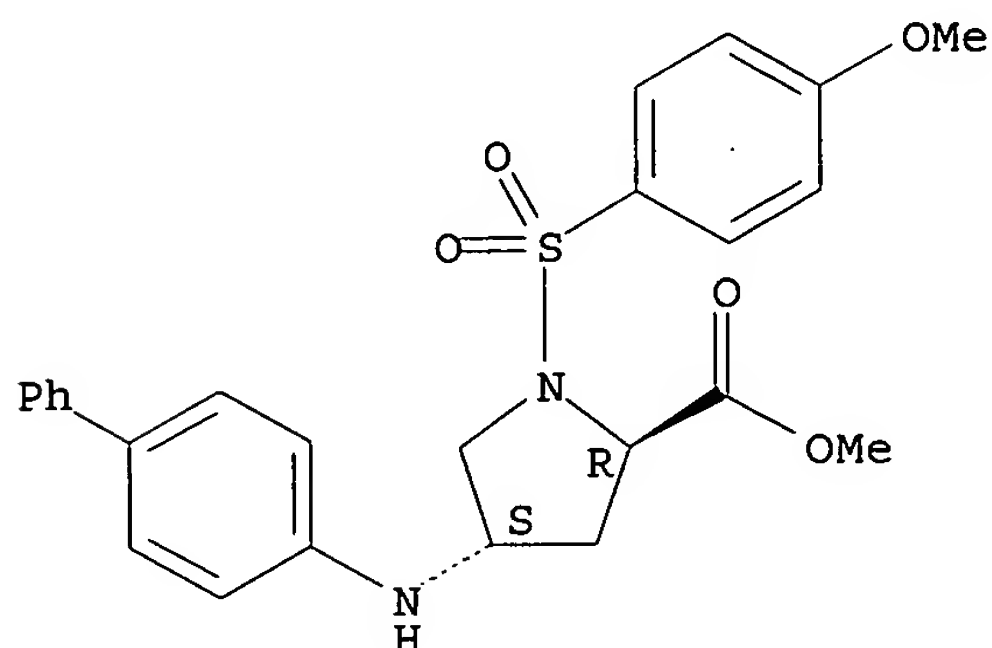
Absolute stereochemistry.



RN 537704-35-1 HCAPLUS

CN D-Proline, 4-([1,1'-biphenyl]-4-ylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

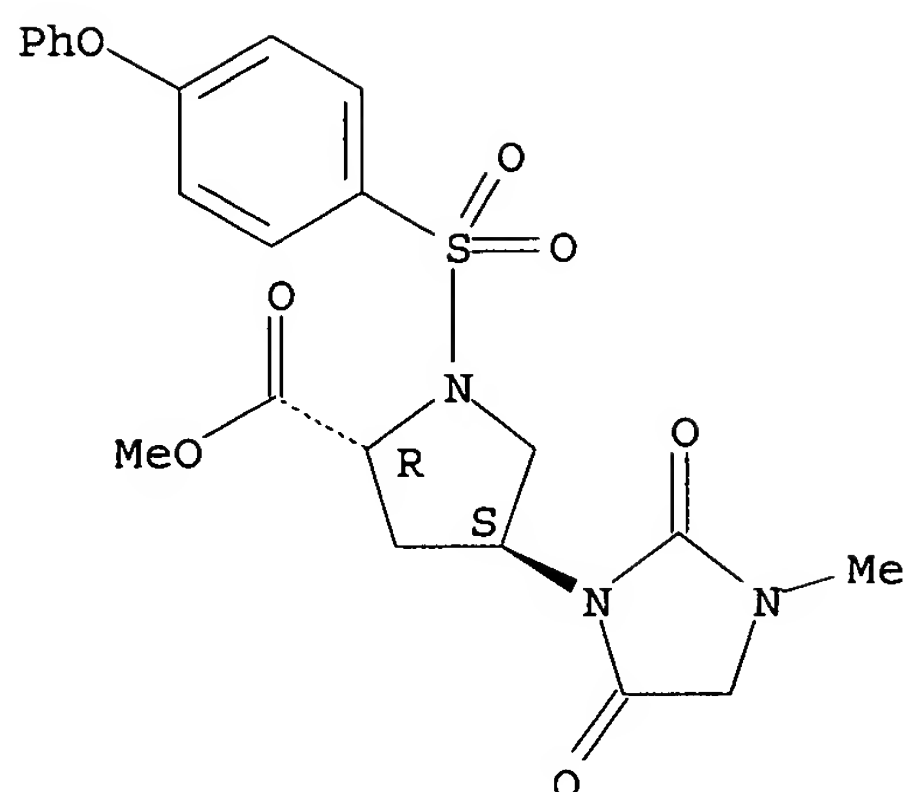
Absolute stereochemistry.



RN 722550-48-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(methylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

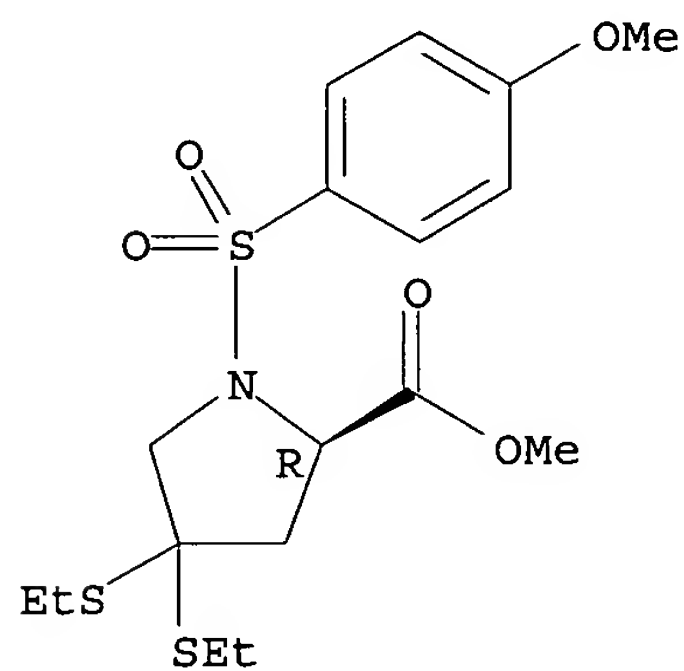
Absolute stereochemistry.



RN 204073-04-1 HCAPLUS

CN D-Proline, 4,4-bis(ethylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester  
(9CI) (CA INDEX NAME)

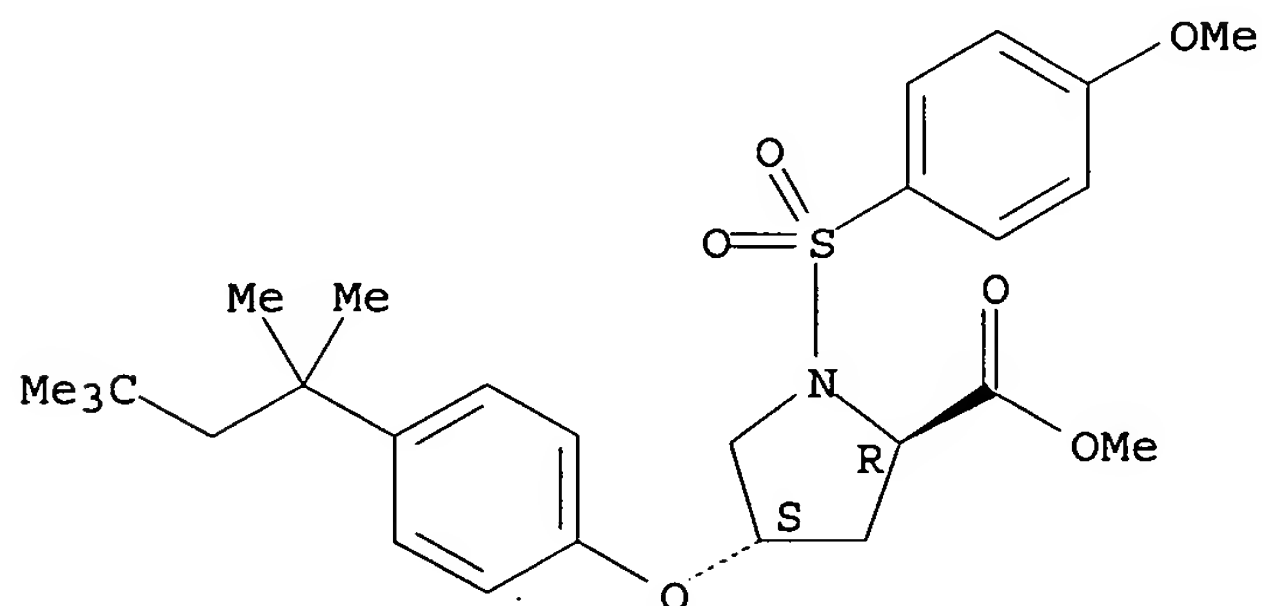
Absolute stereochemistry.



RN 537704-28-2 HCAPLUS

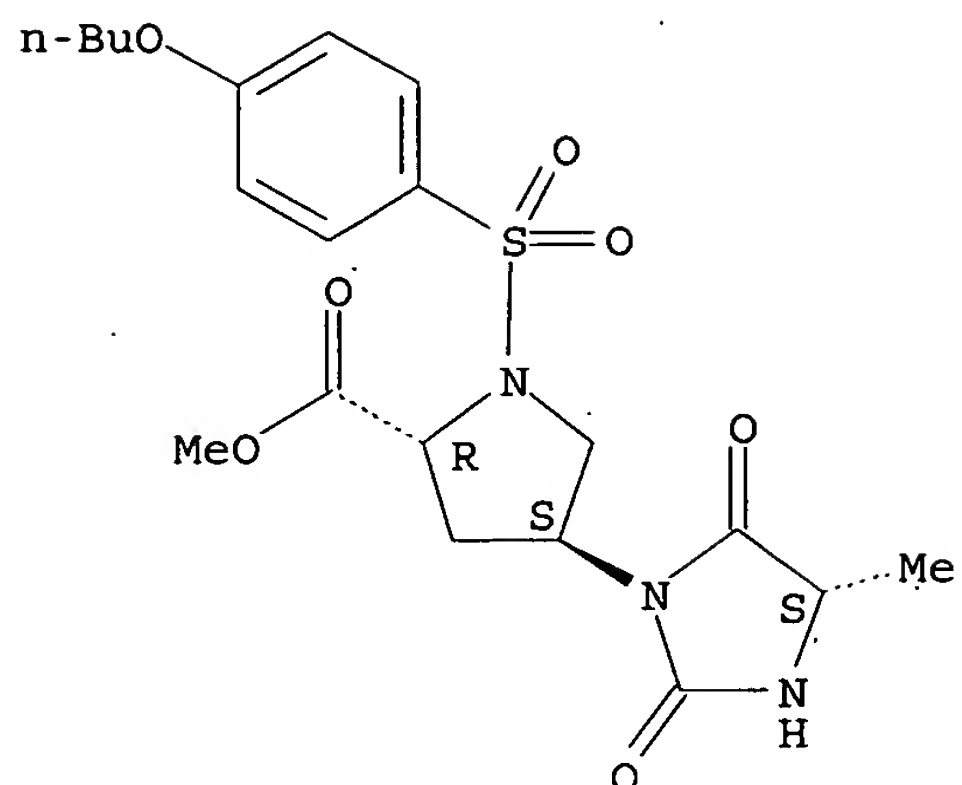
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 537704-32-8 HCAPLUS

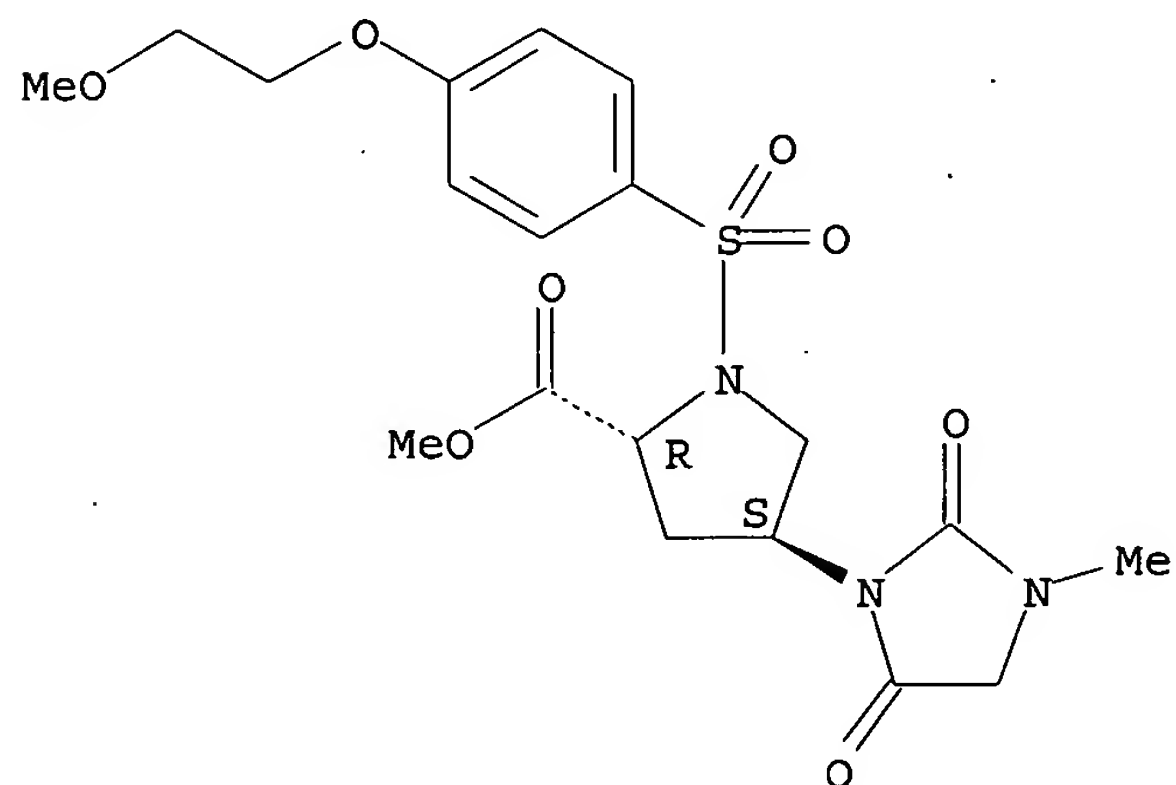




RN 204072-99-1 HCAPLUS

CN D-Proline, 1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

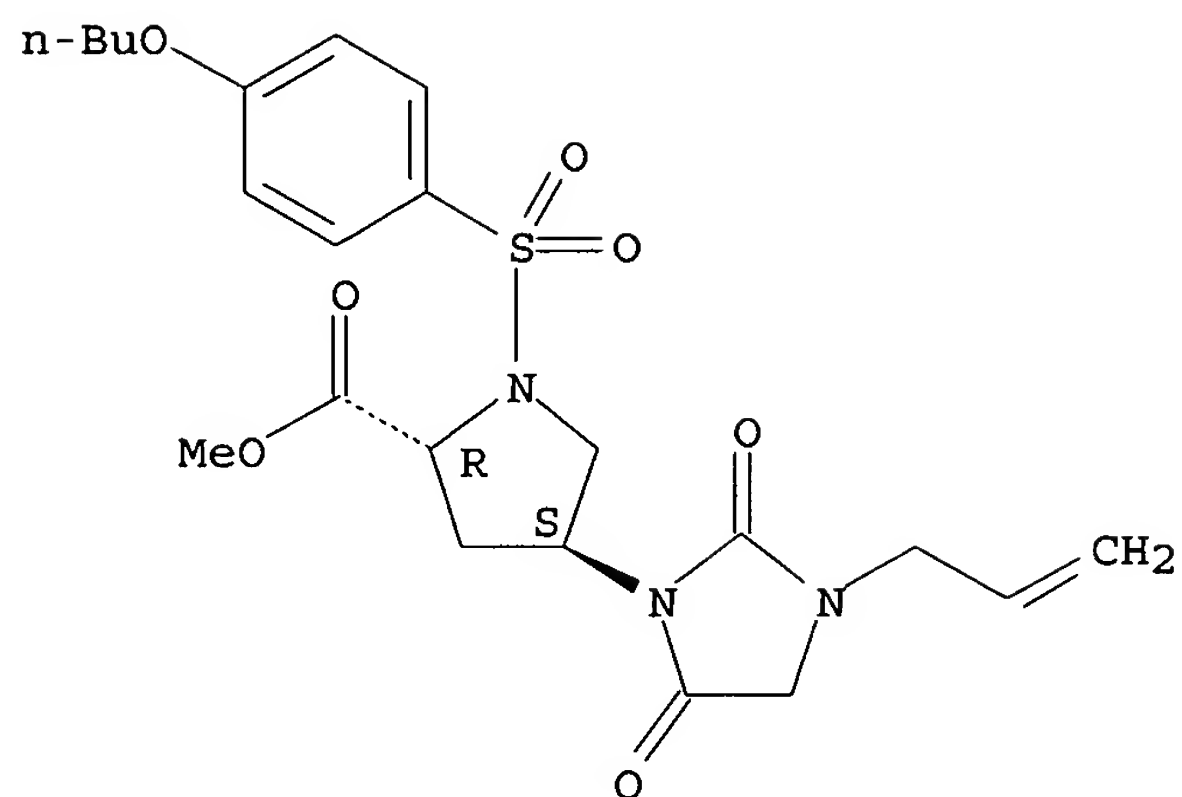
Absolute stereochemistry.



RN 204073-00-7 HCAPLUS

CN D-Proline, 4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-1-[[4-(3-methoxypropoxy)phenyl]sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

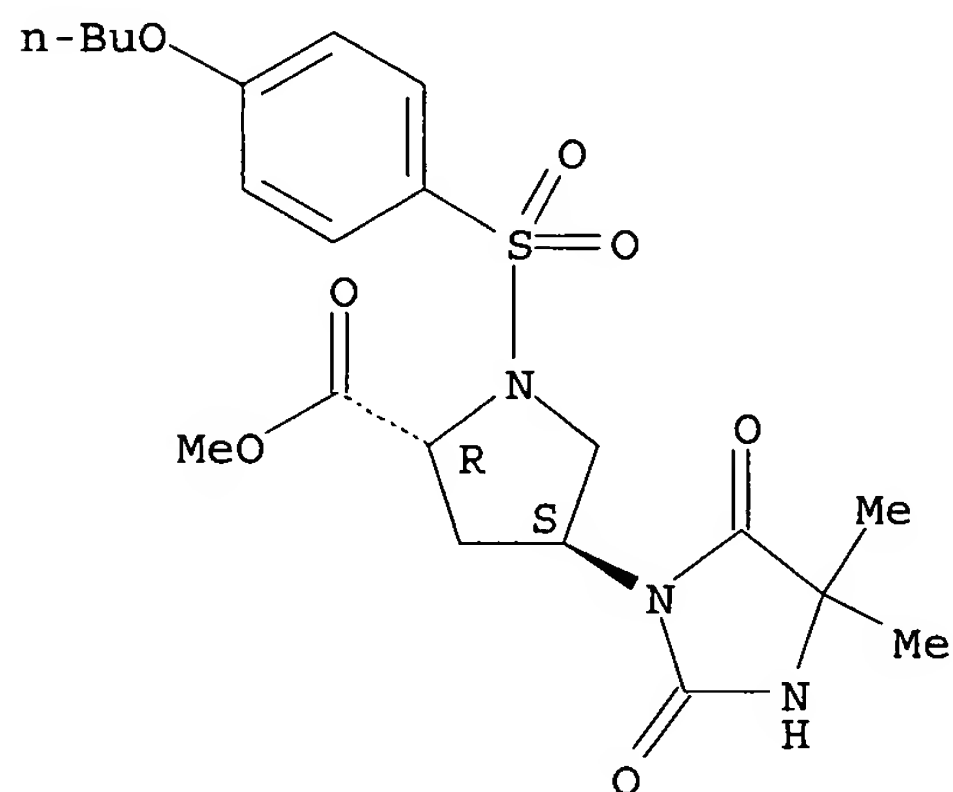
Absolute stereochemistry.



RN 204072-97-9 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

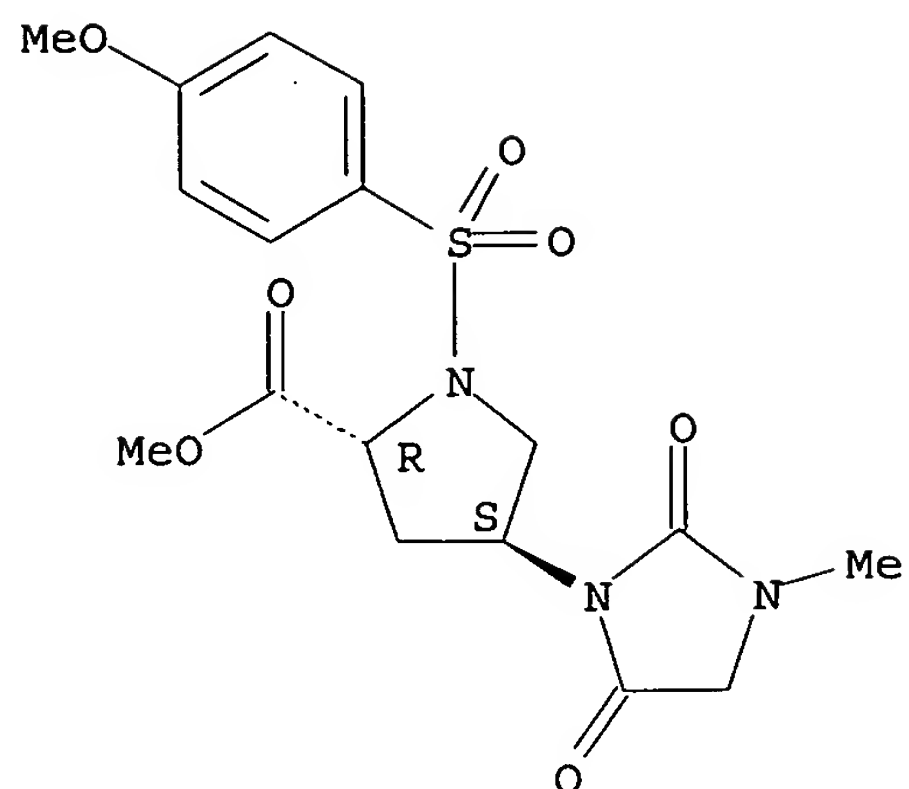
Absolute stereochemistry.



RN 204072-98-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(4S)-4-methyl-2,5-dioxo-1-imidazolidinyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

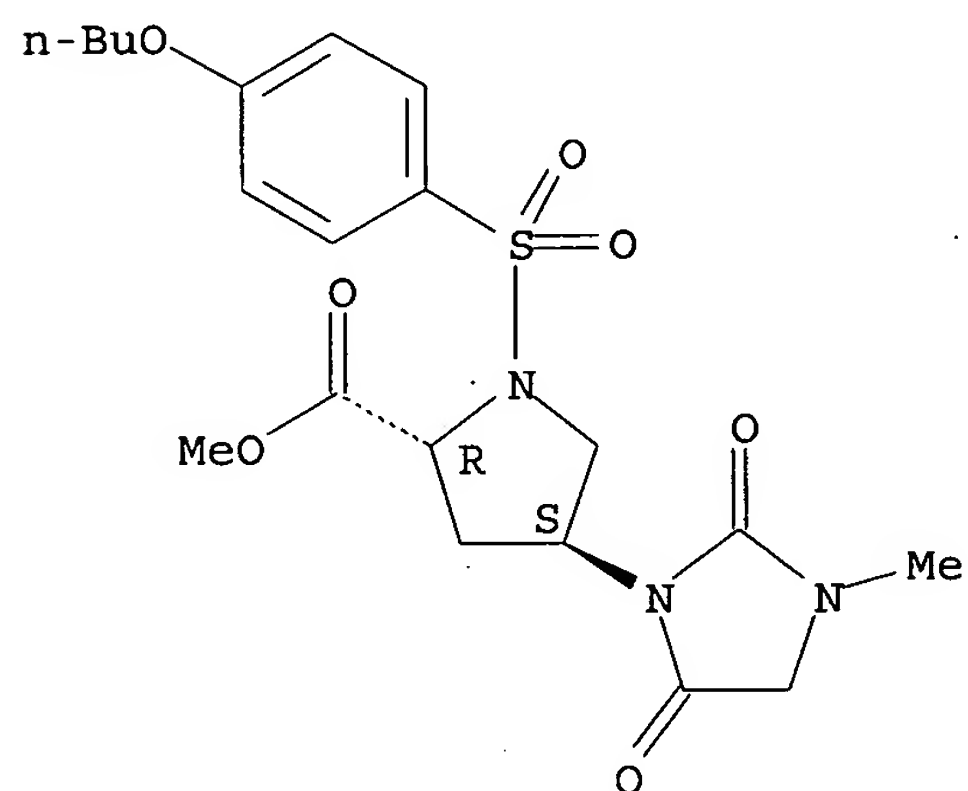
Absolute stereochemistry.



RN 204072-95-7 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

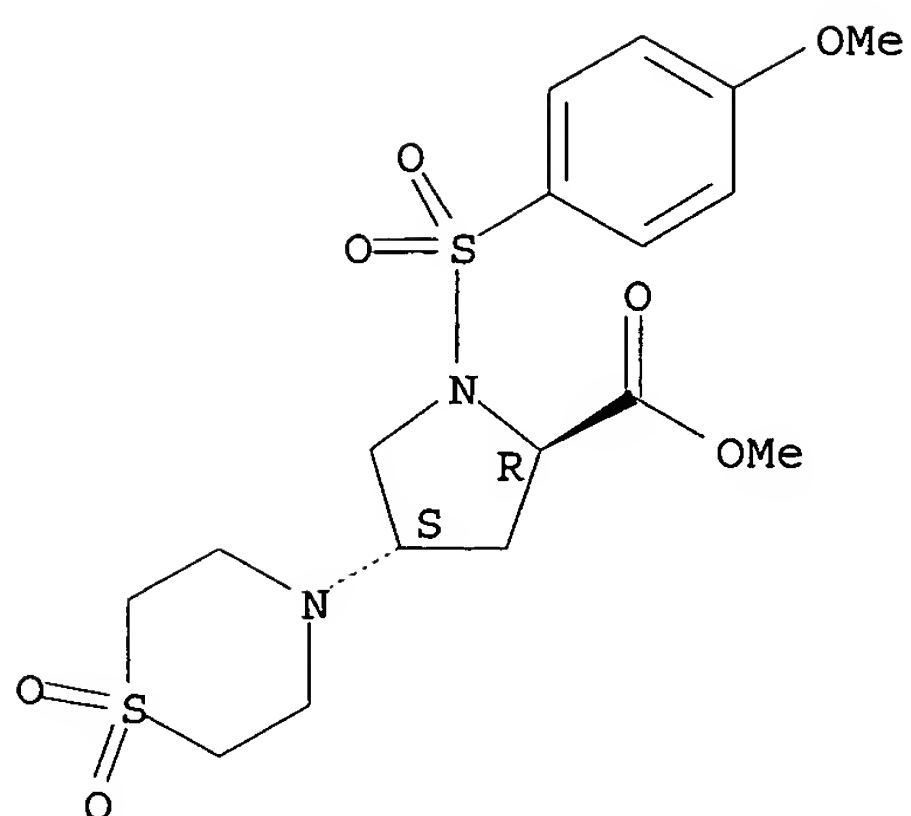
Absolute stereochemistry..



RN 204072-96-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[2,5-dioxo-3-(2-propenyl)-1-imidazolidinyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

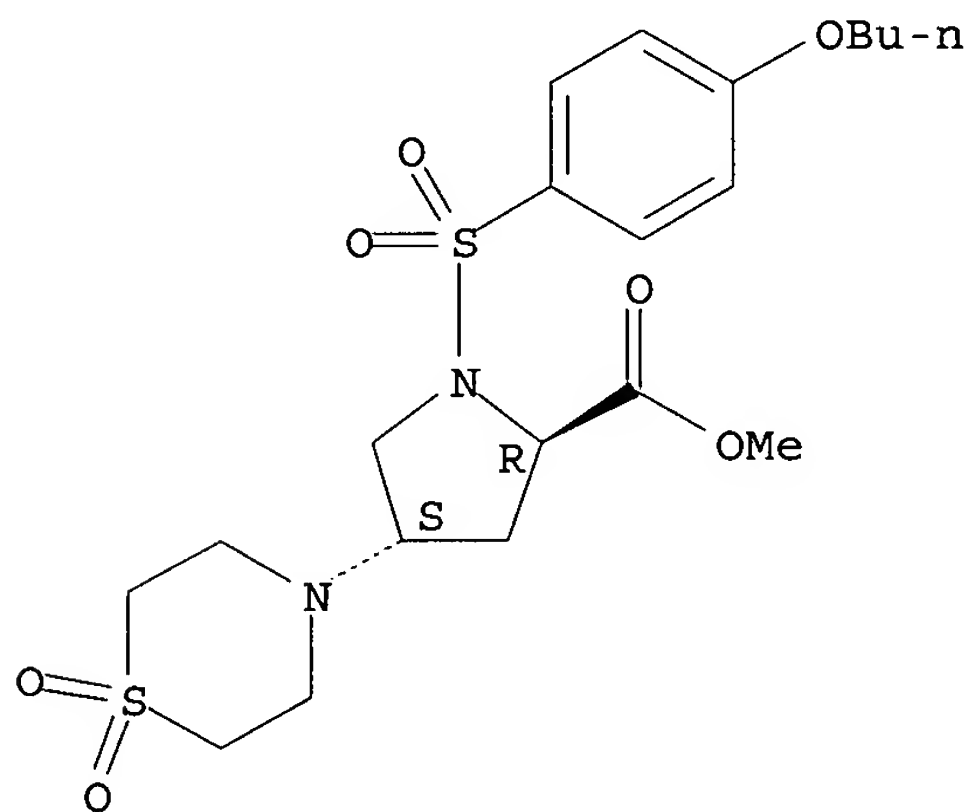
Absolute stereochemistry.



RN 204072-93-5 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1,1-dioxido-4-thiomorpholinyl)-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

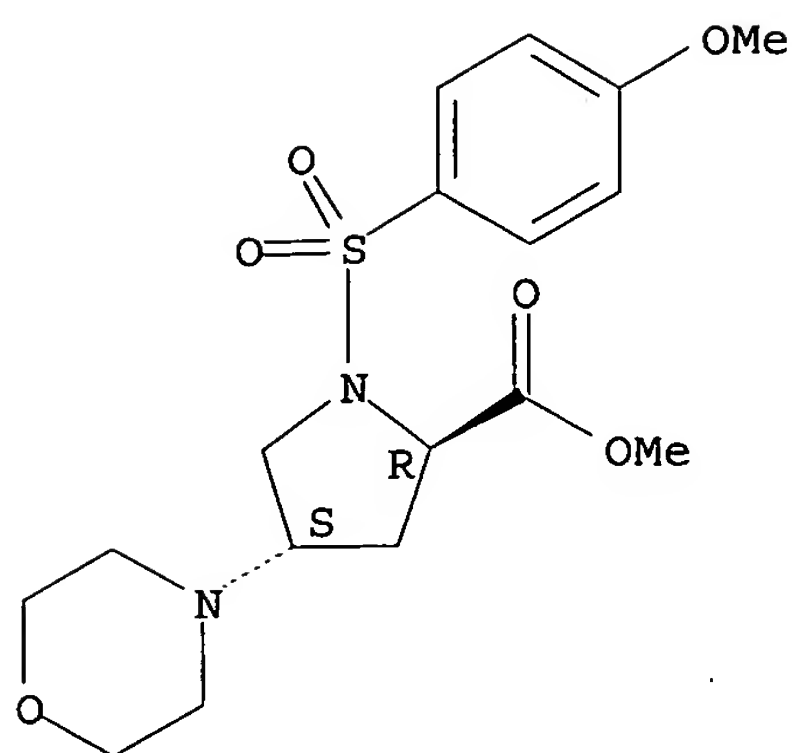
Absolute stereochemistry.



RN 204072-94-6 HCAPLUS

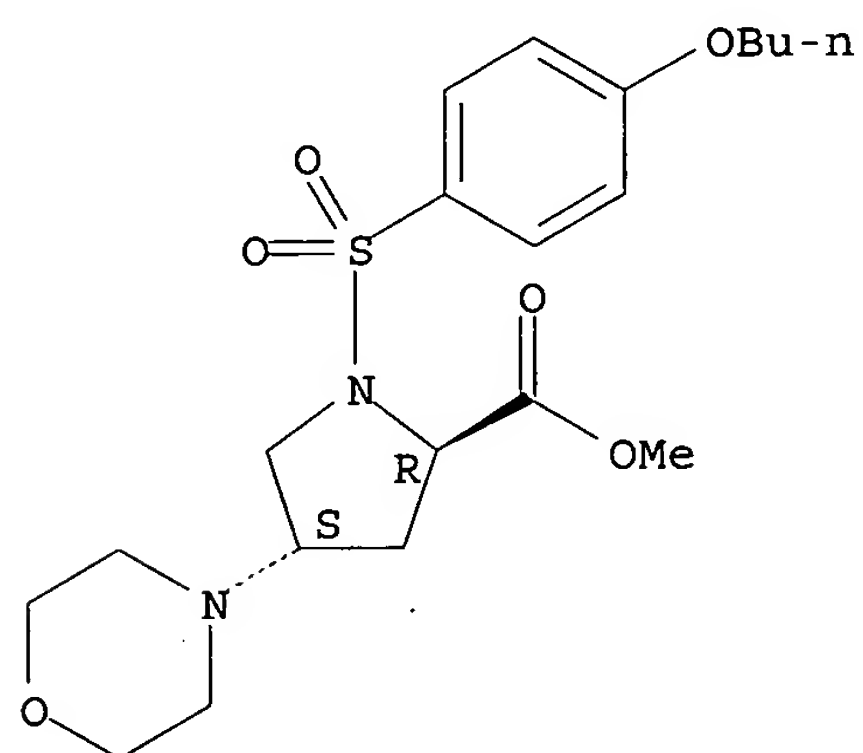
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



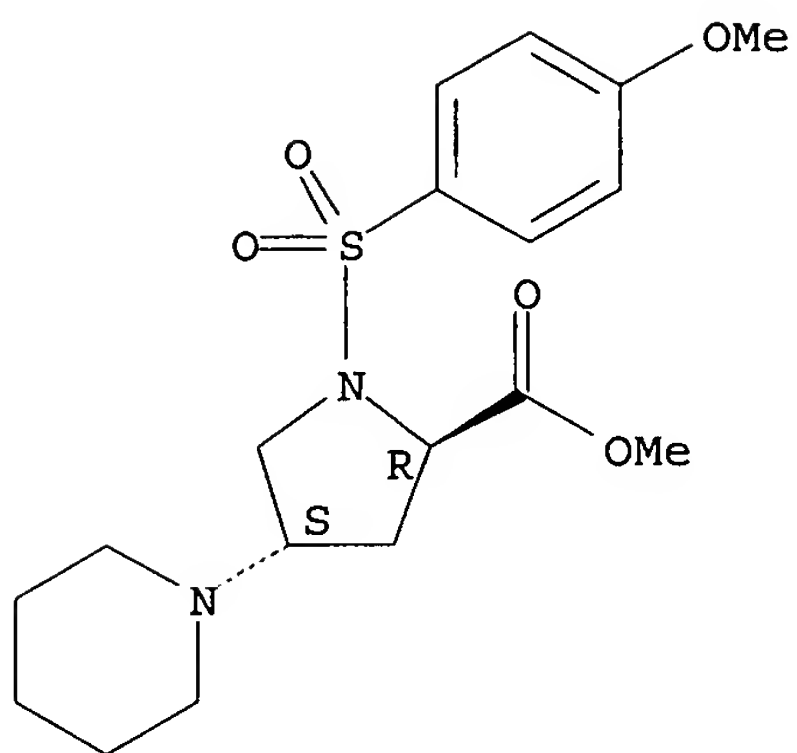
RN 204072-91-3 HCAPLUS  
 CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, methyl ester,  
 (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



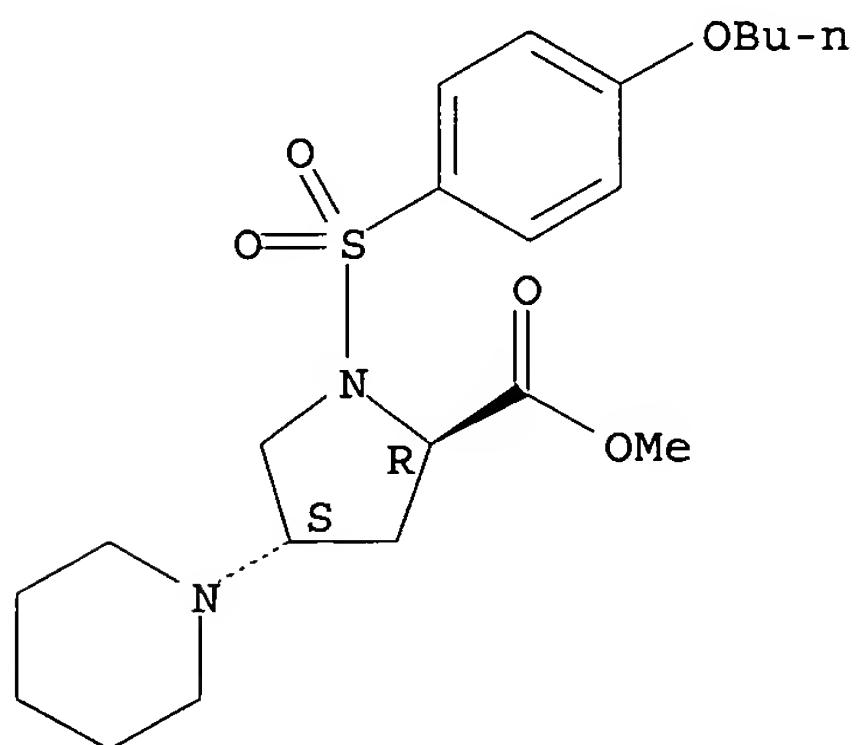
RN 204072-92-4 HCAPLUS  
 CN D-Proline, 4-(1,1-dioxido-4-thiomorpholinyl)-1-[(4-methoxyphenyl)sulfonyl]-  
 , methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



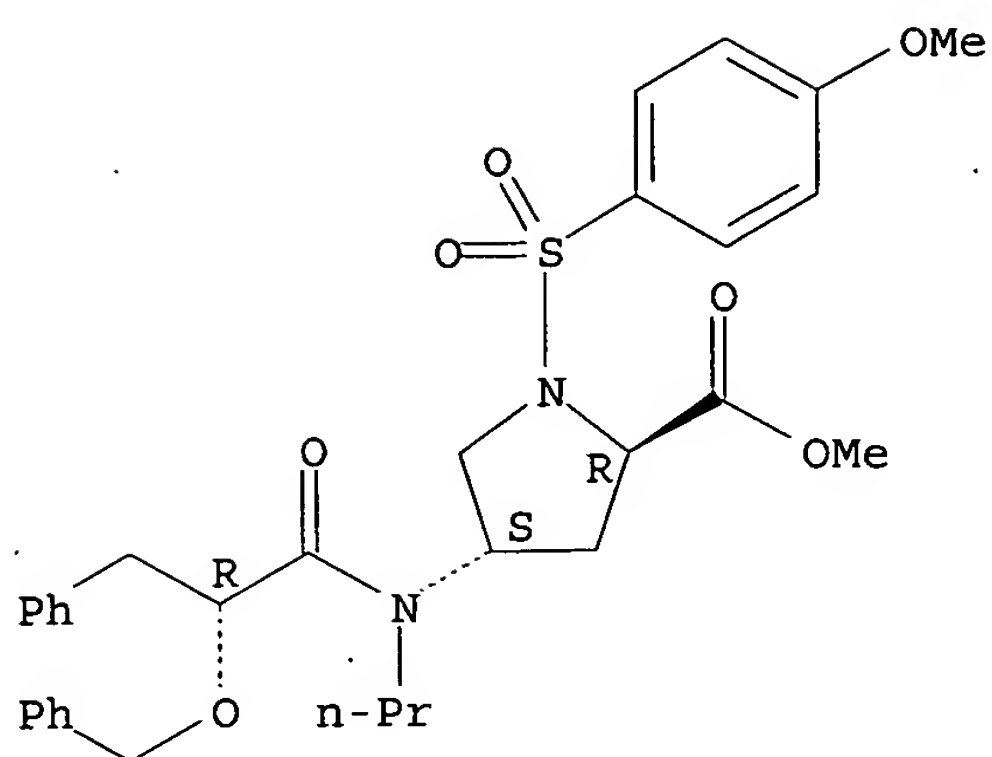
RN 204072-89-9 HCAPLUS  
 CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, methyl ester,  
 (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-90-2 HCAPLUS  
 CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, methyl ester,  
 (4S)- (9CI) (CA INDEX NAME)

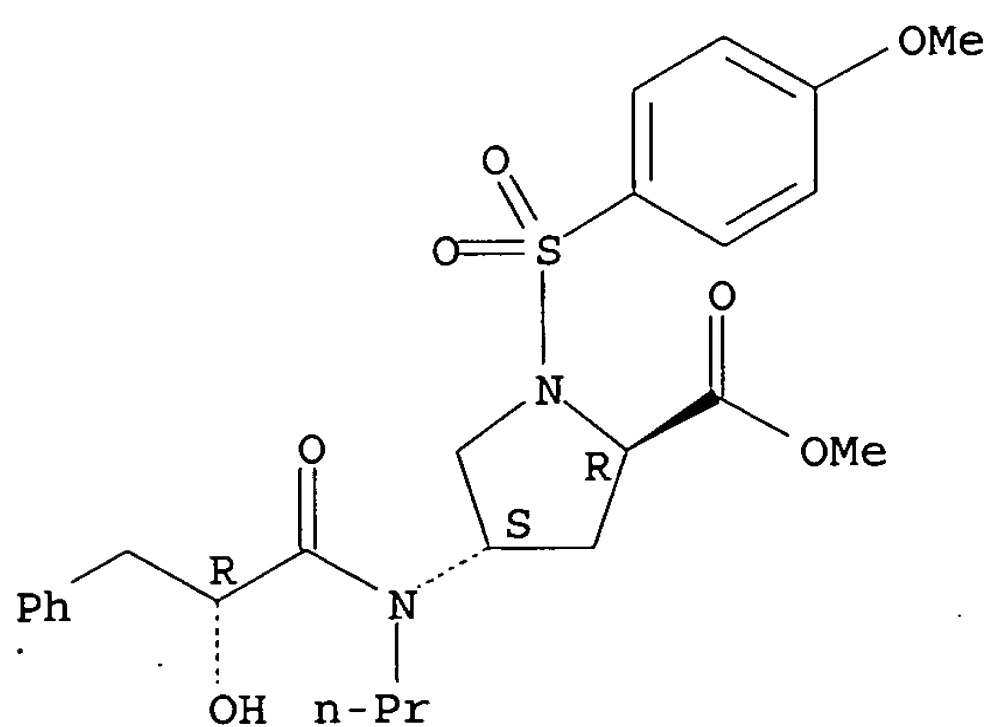
Absolute stereochemistry.



RN 204072-87-7 HCAPLUS

CN D-Proline, 4-[[[(2R)-2-hydroxy-1-oxo-3-phenylpropyl]propylamino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

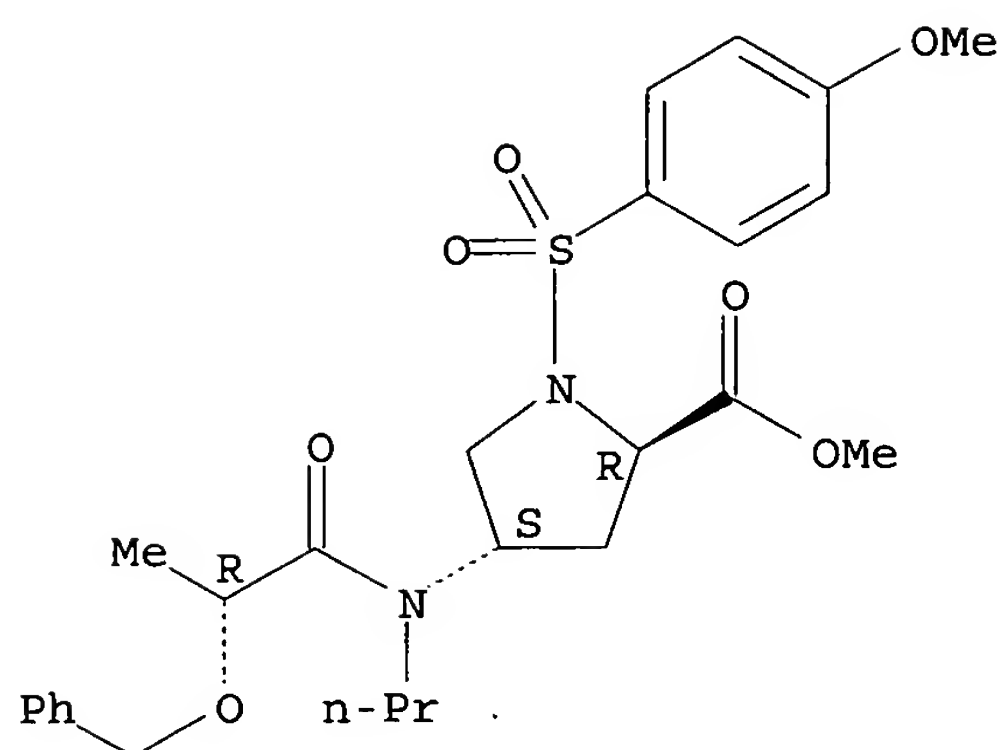
Absolute stereochemistry.



RN 204072-88-8 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

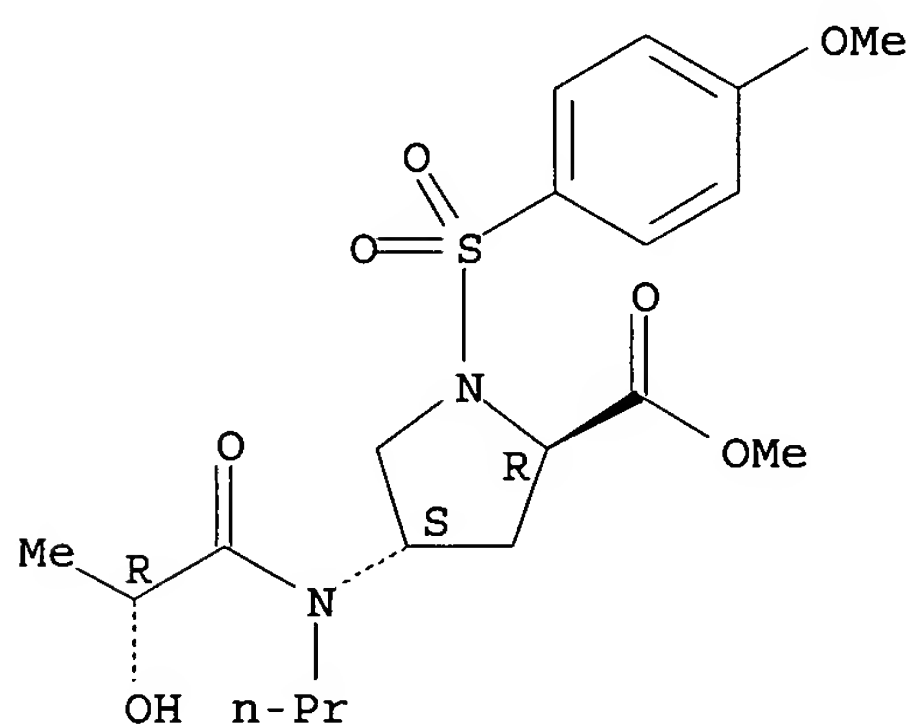
Absolute stereochemistry.



RN 204072-85-5 HCAPLUS

CN D-Proline, 4-[[[(2R)-2-hydroxy-1-oxopropyl]propylamino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-86-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[[(2R)-1-oxo-3-phenyl-2-(phenylmethoxy)propyl]propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

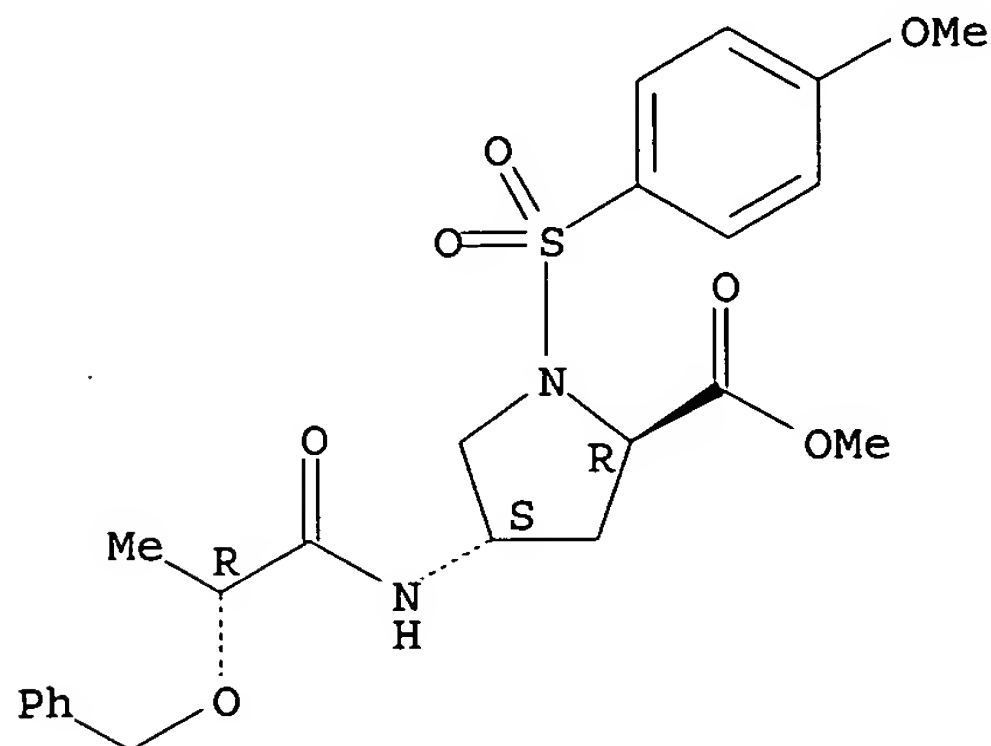
Absolute stereochemistry.



RN 204072-82-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[ (2R)-1-oxo-2-(phenylmethoxy)propyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

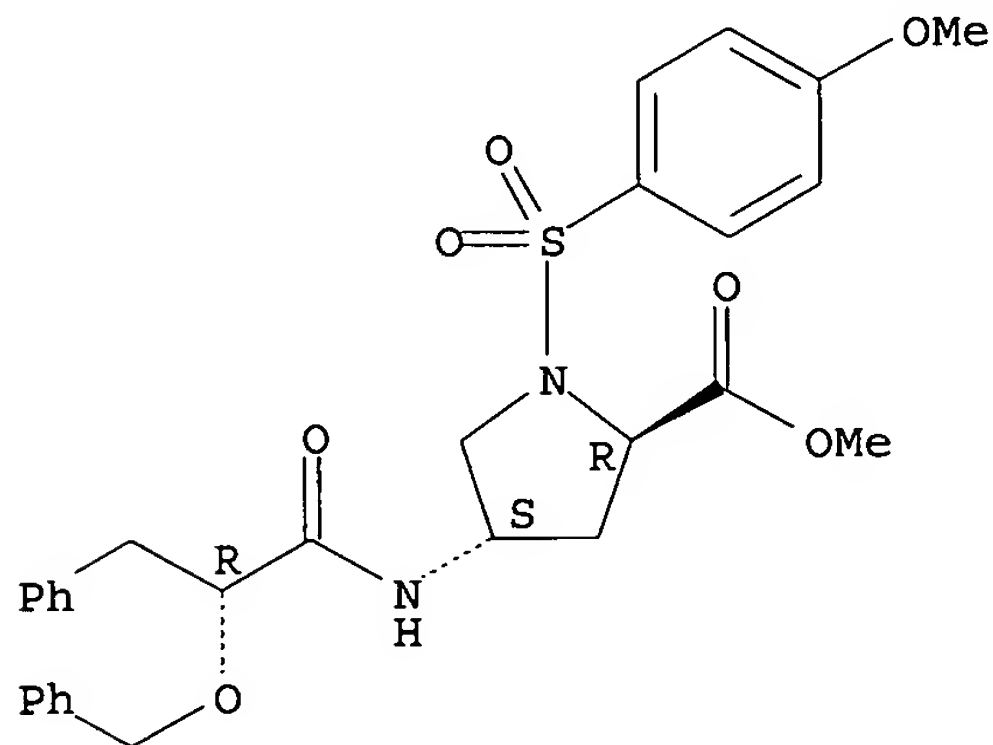
Absolute stereochemistry.



RN 204072-83-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[ (2R)-1-oxo-3-phenyl-2-(phenylmethoxy)propyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

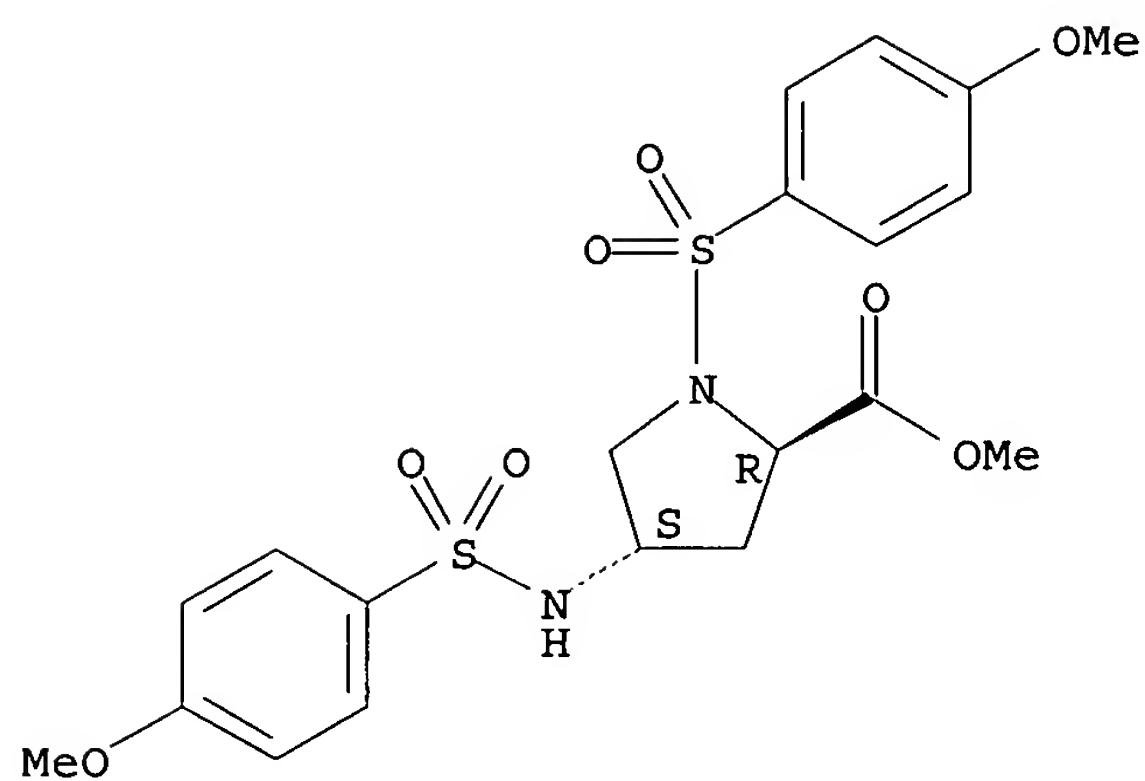
Absolute stereochemistry.



RN 204072-84-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[ (2R)-1-oxo-2-(phenylmethoxy)propyl]propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

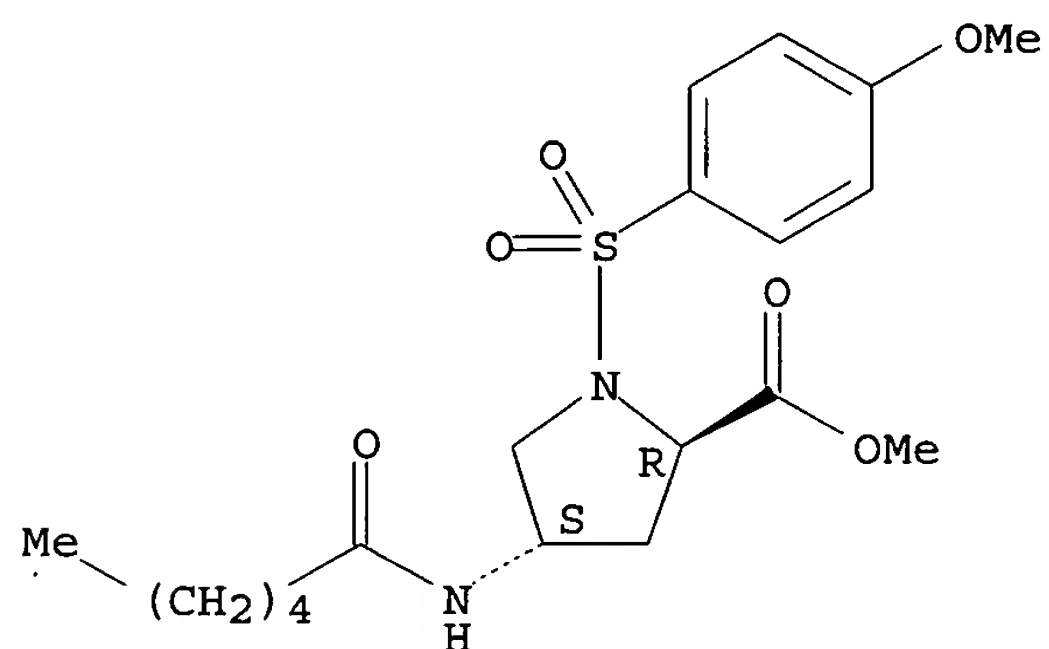
Absolute stereochemistry.



RN 204072-79-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-oxohexyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

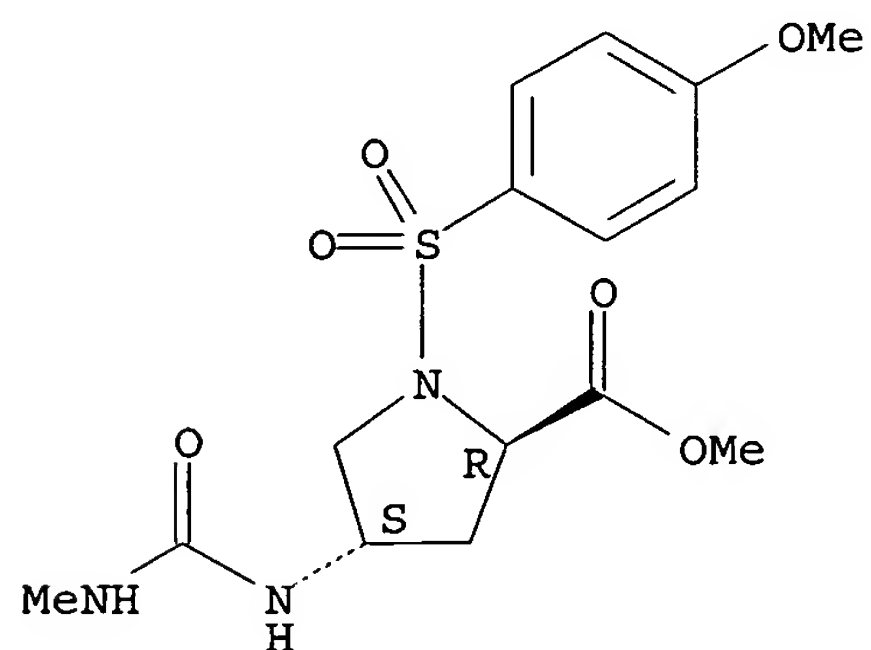
Absolute stereochemistry.

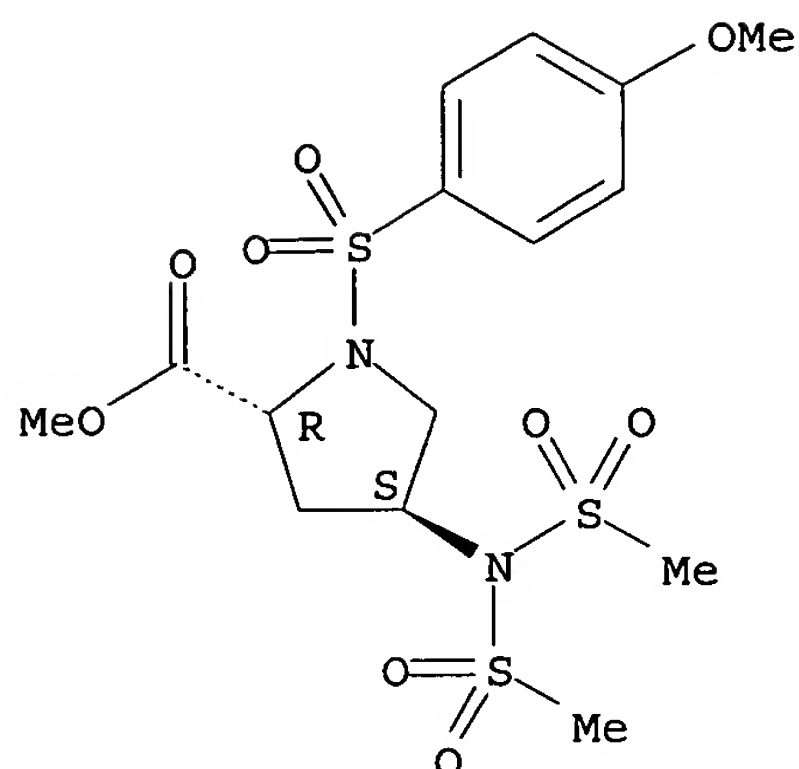


RN 204072-81-1 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[[(methylamino)carbonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

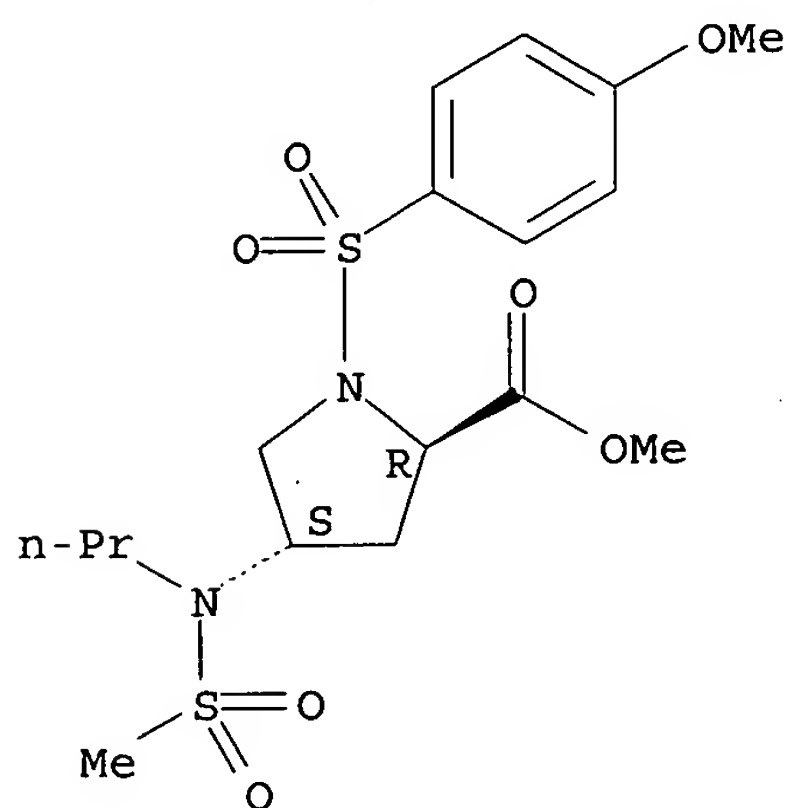




RN 204072-77-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-78-6 HCAPLUS

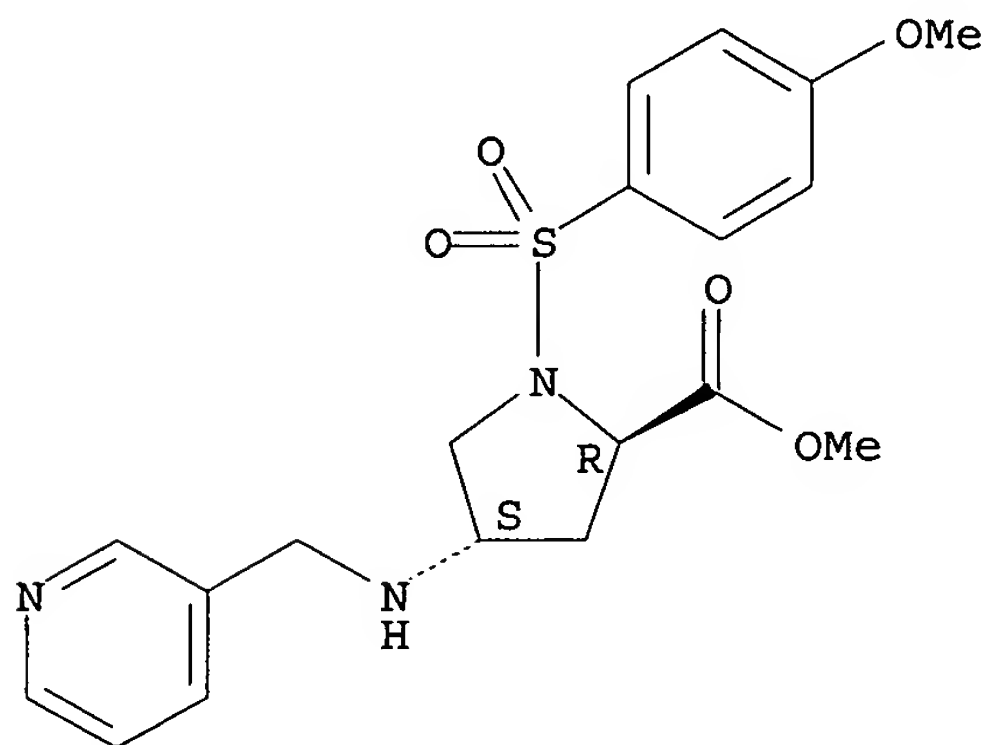
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[4-methoxyphenyl)sulfonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 204072-74-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(3-pyridinylmethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

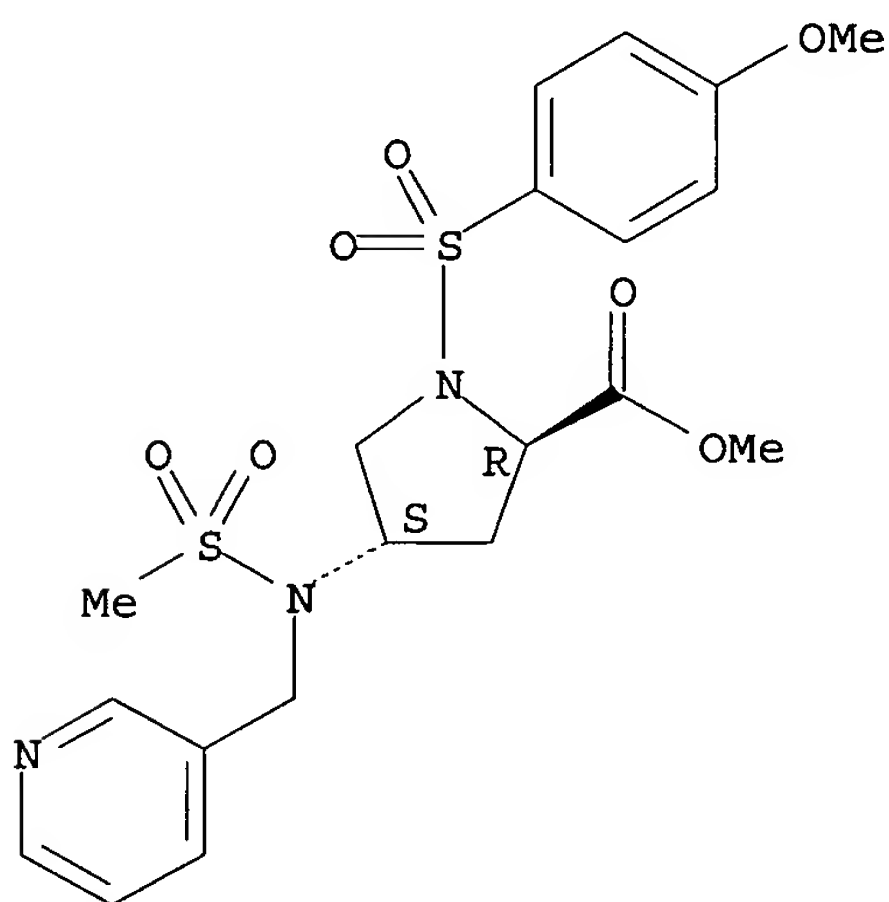
Absolute stereochemistry.



RN 204072-75-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)(3-pyridinylmethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

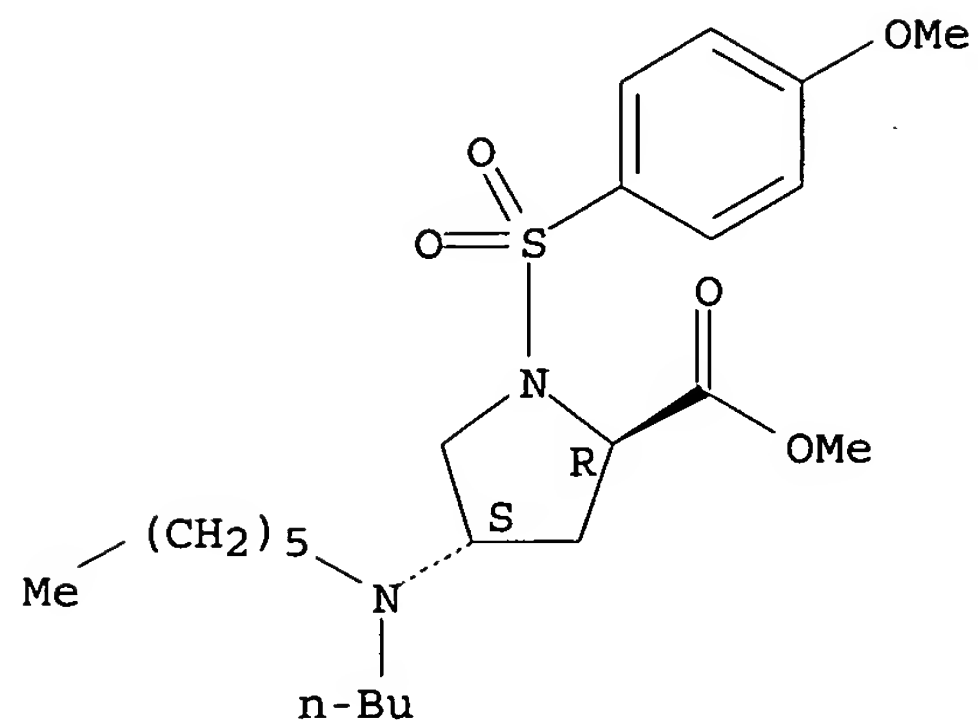


RN 204072-76-4 HCAPLUS

CN D-Proline, 4-[bis(methylsulfonyl)amino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

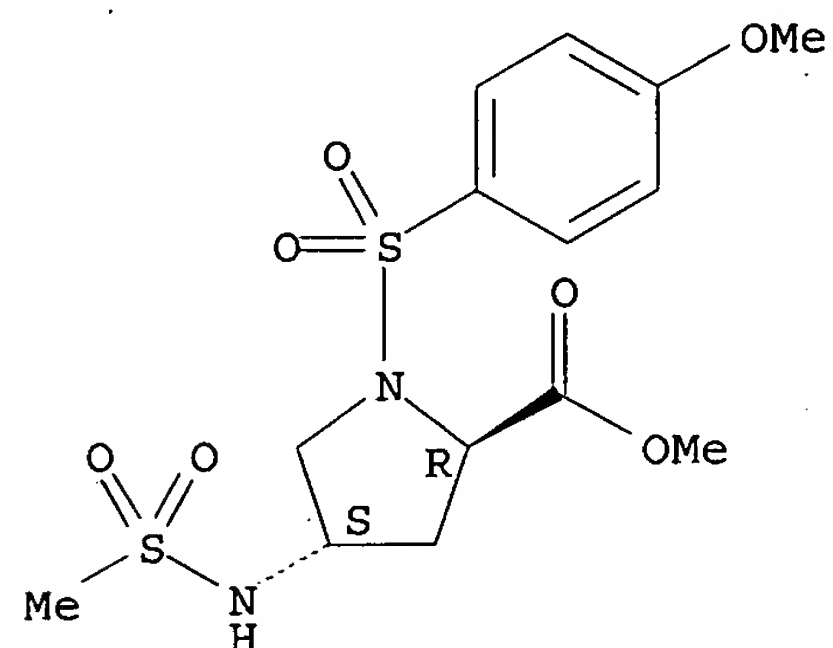
Absolute stereochemistry.



RN 204072-71-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

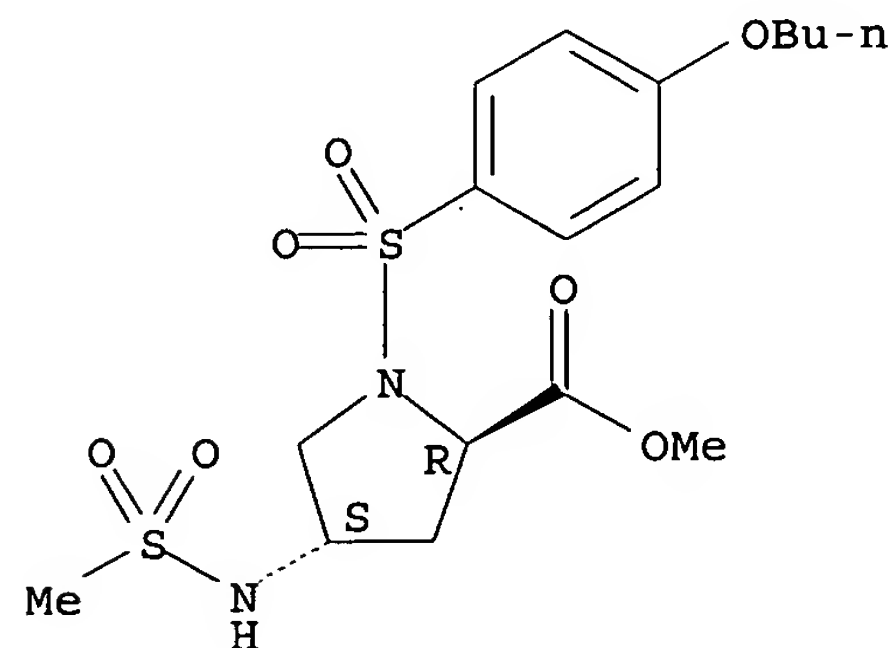
Absolute stereochemistry.

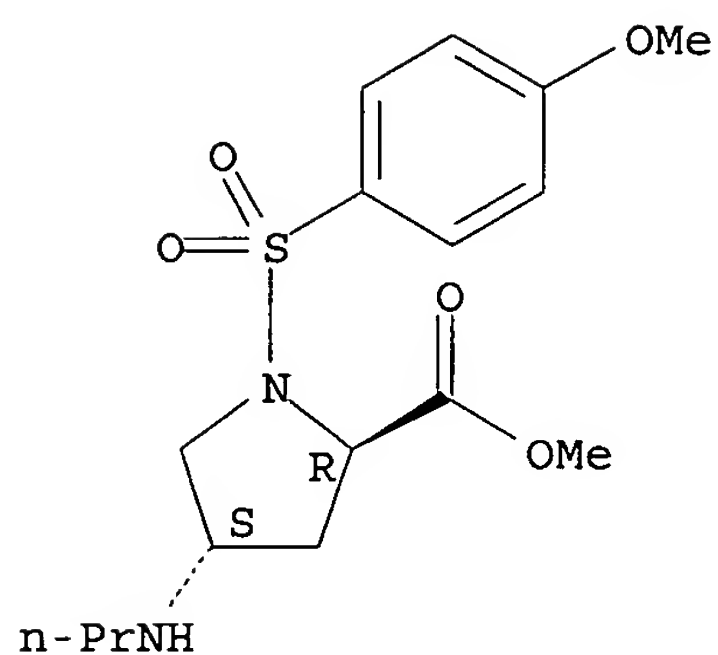


RN 204072-72-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(methylsulfonyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

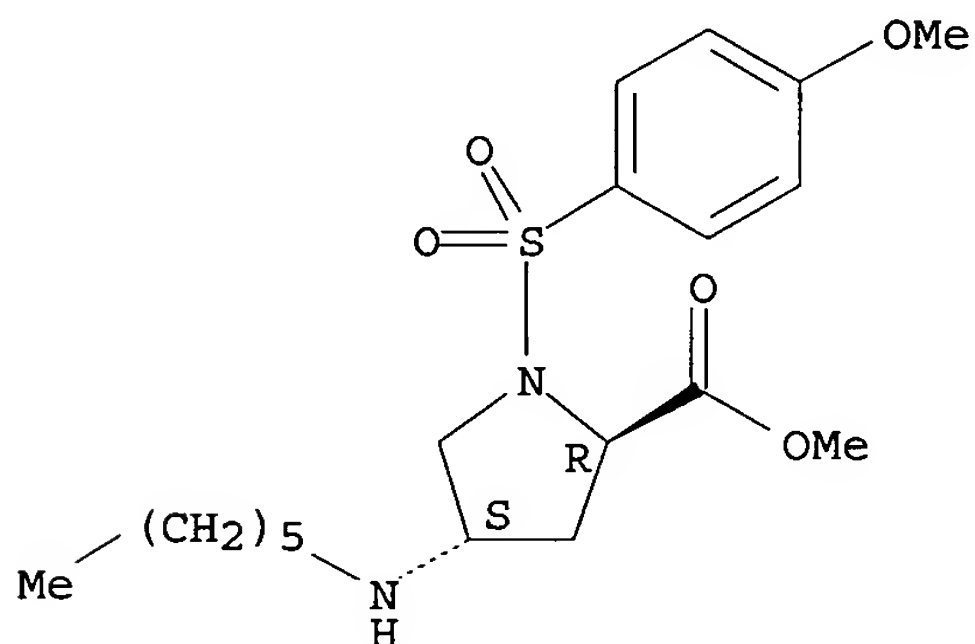




RN 204072-68-4 HCAPLUS

CN D-Proline, 4-(hexylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

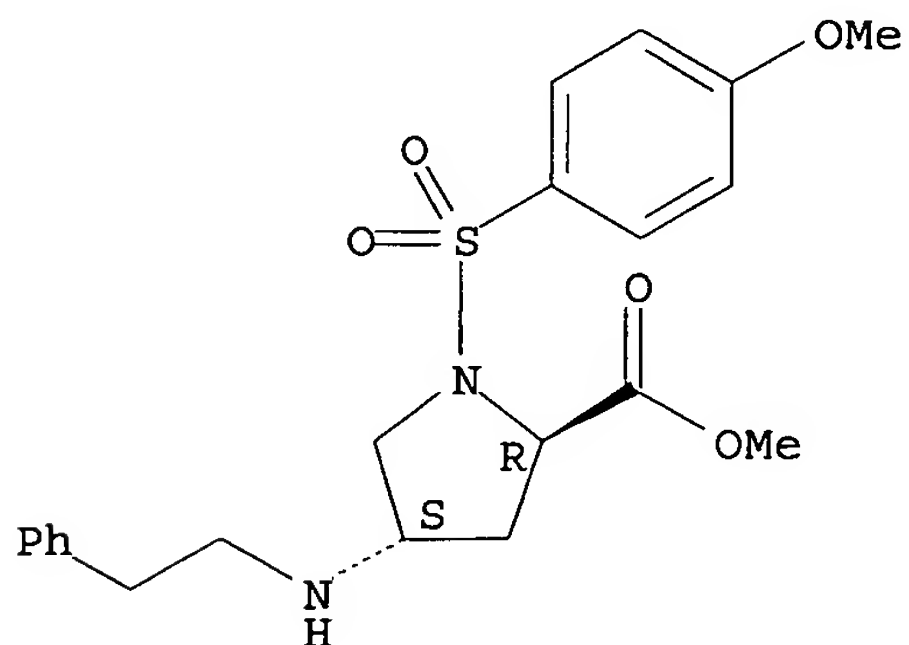
Absolute stereochemistry.



RN 204072-69-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(2-phenylethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



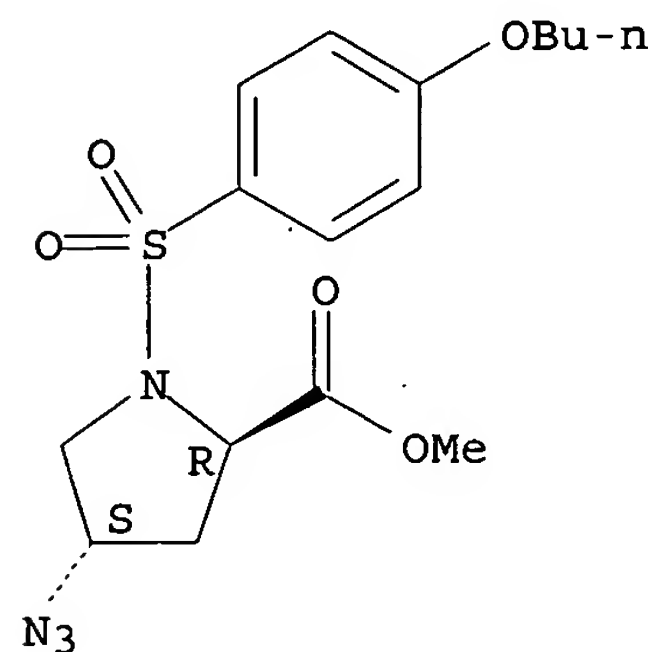
RN 204072-70-8 HCAPLUS

CN D-Proline, 4-(butylhexylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

RN 204072-65-1 HCAPLUS

CN D-Proline, 4-azido-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

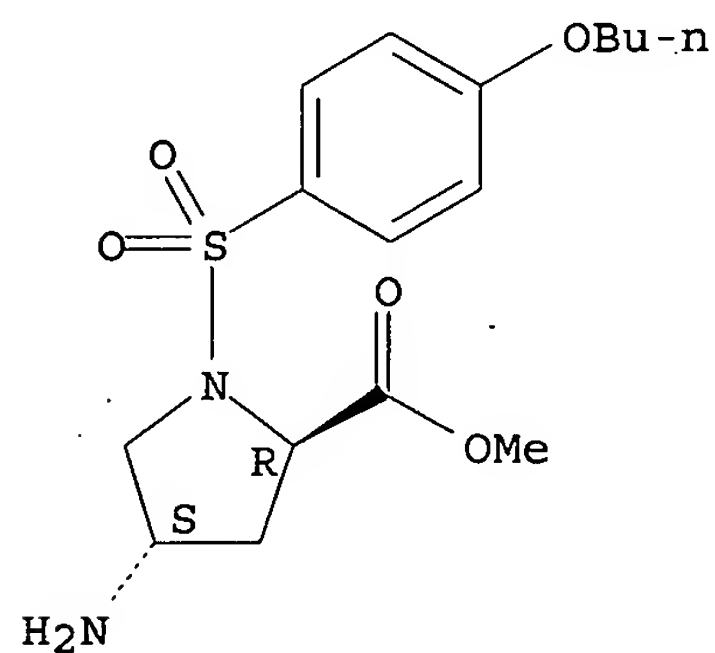
Absolute stereochemistry.



RN 204072-66-2 HCAPLUS

CN D-Proline, 4-amino-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



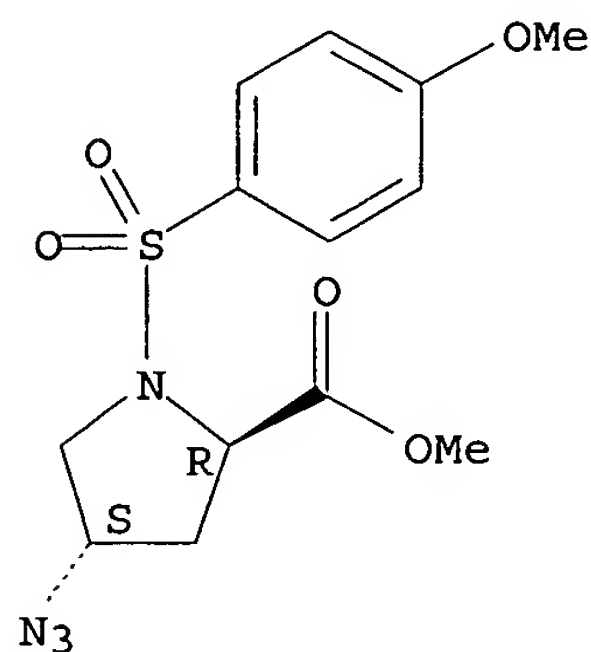
RN 204072-67-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(propylamino)-, methyl ester,  
(4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

(9CI) (CA INDEX NAME)

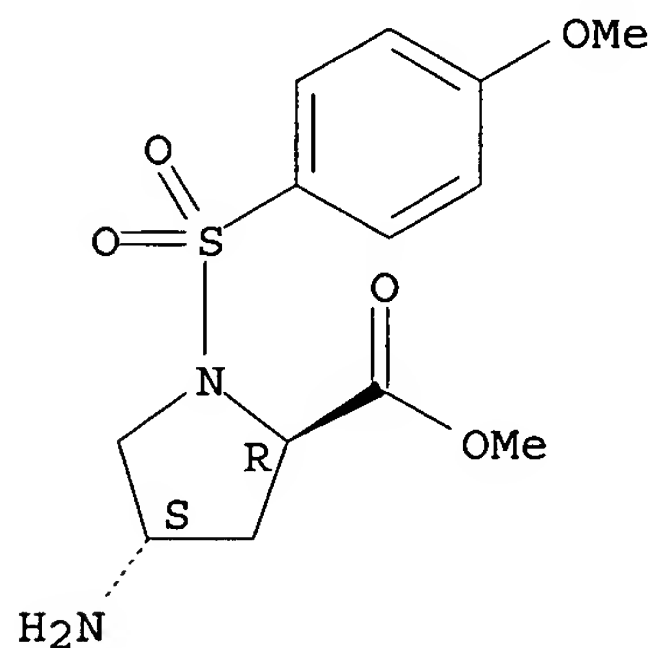
Absolute stereochemistry.



RN 204072-63-9 HCAPLUS

CN D-Proline, 4-amino-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

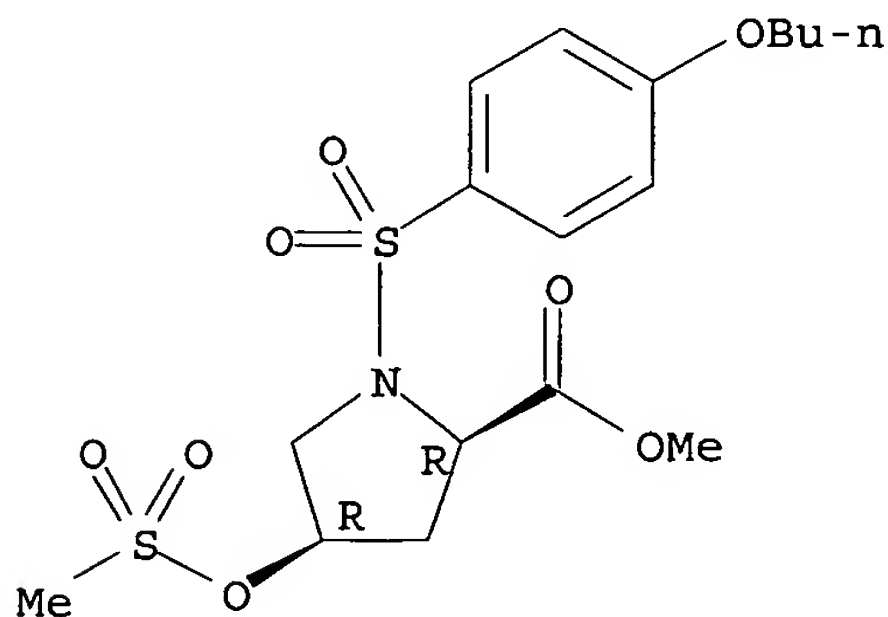
Absolute stereochemistry.



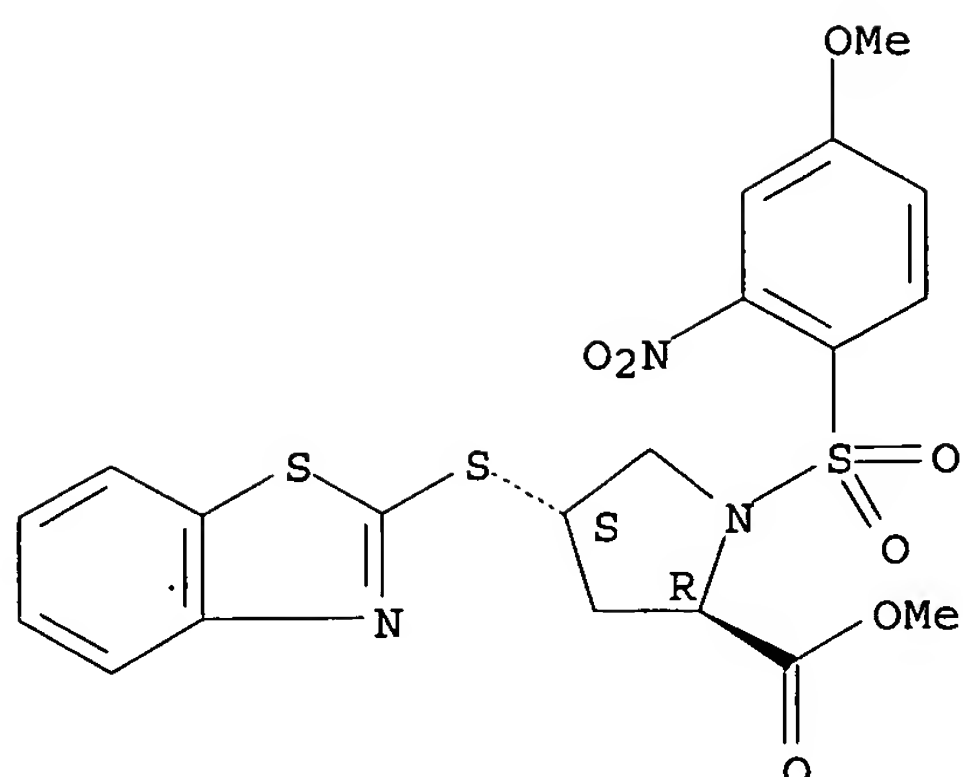
RN 204072-64-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(methylsulfonyl)oxy]-, methyl  
ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

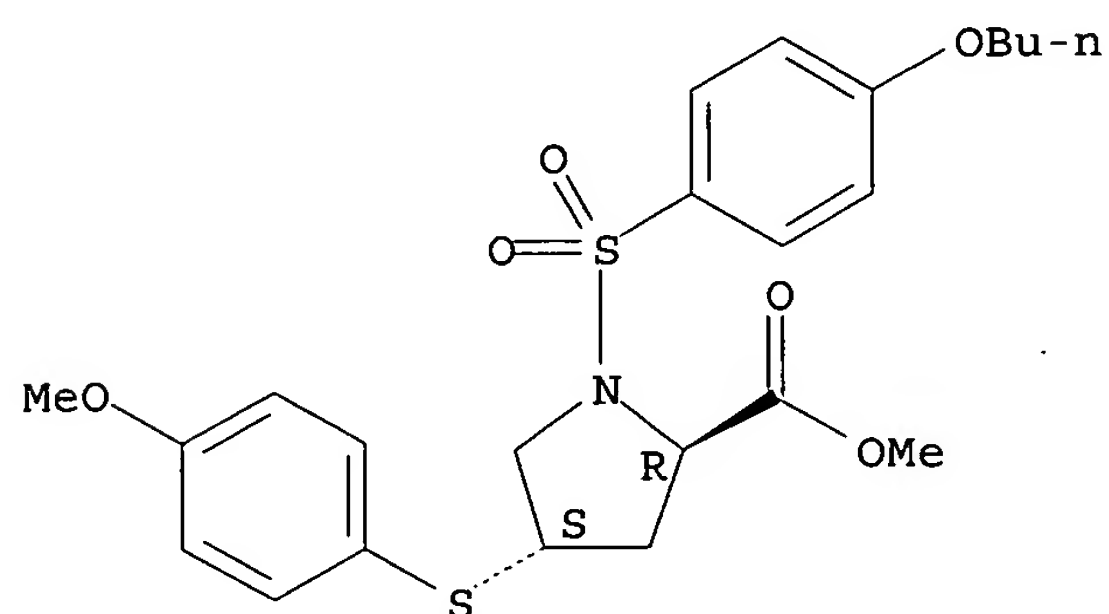






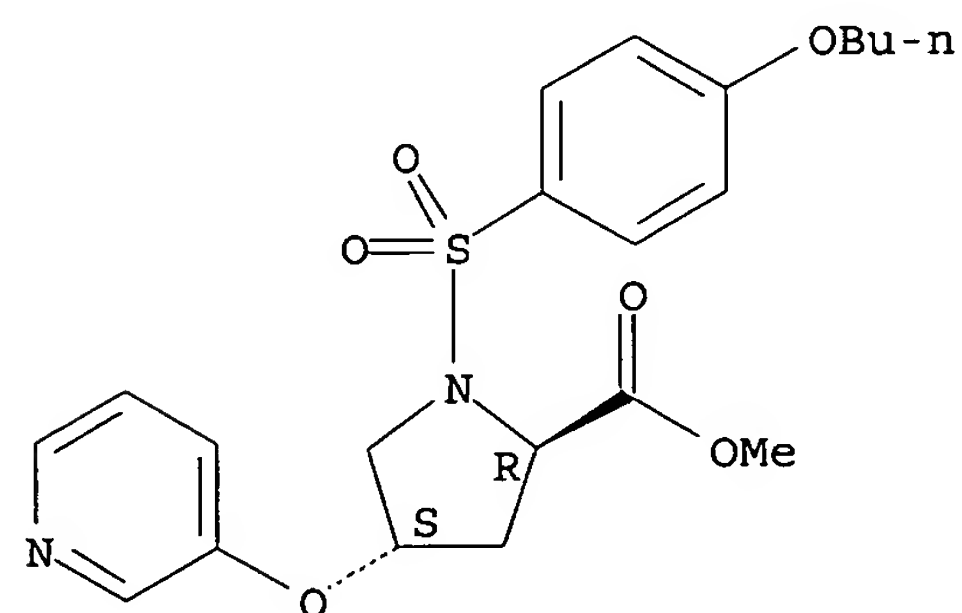
RN 204072-60-6 HCAPLUS  
 CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(4-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-61-7 HCAPLUS  
 CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(3-pyridinyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

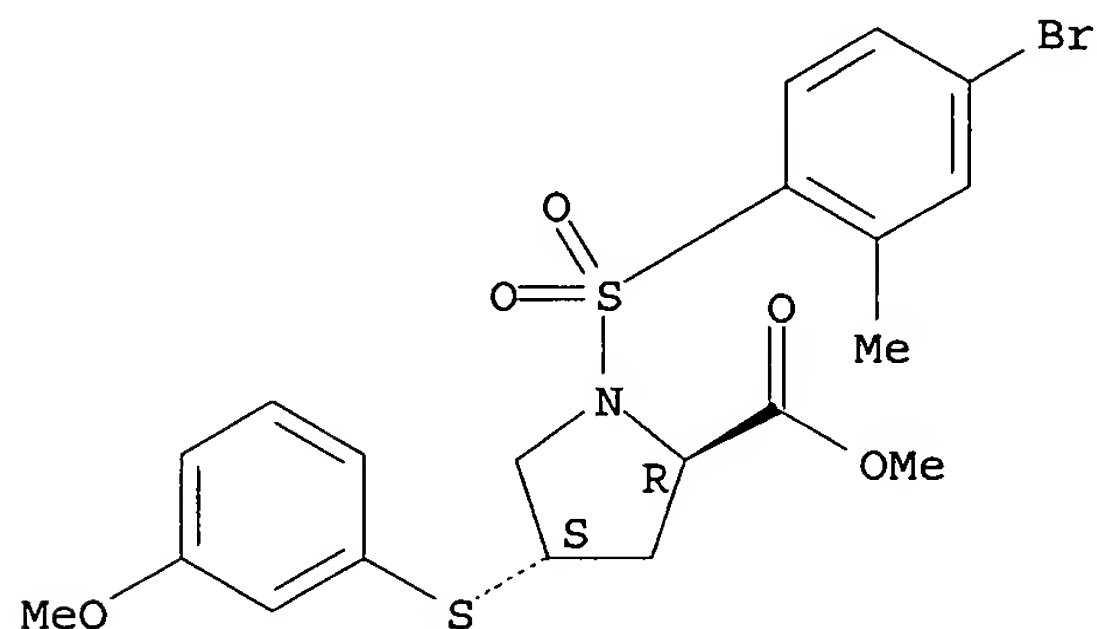


RN 204072-62-8 HCAPLUS  
 CN D-Proline, 4-azido-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-

RN 204072-57-1 HCAPLUS

CN D-Proline, 1-[(4-bromo-2-methylphenyl)sulfonyl]-4-[(3-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

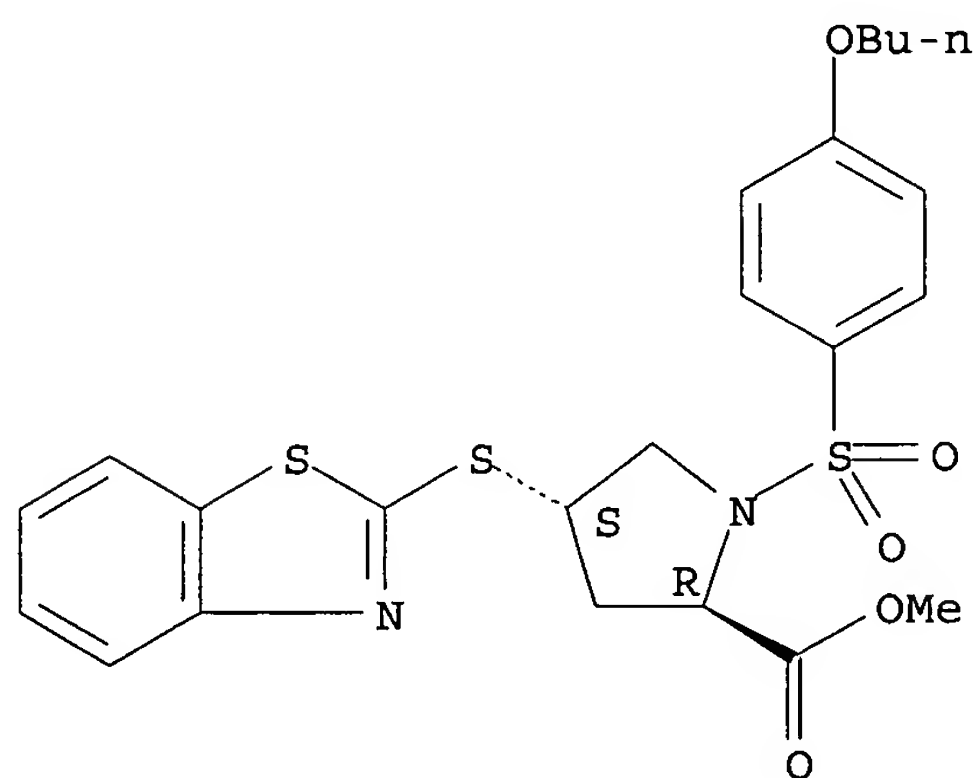
Absolute stereochemistry.



RN 204072-58-2 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



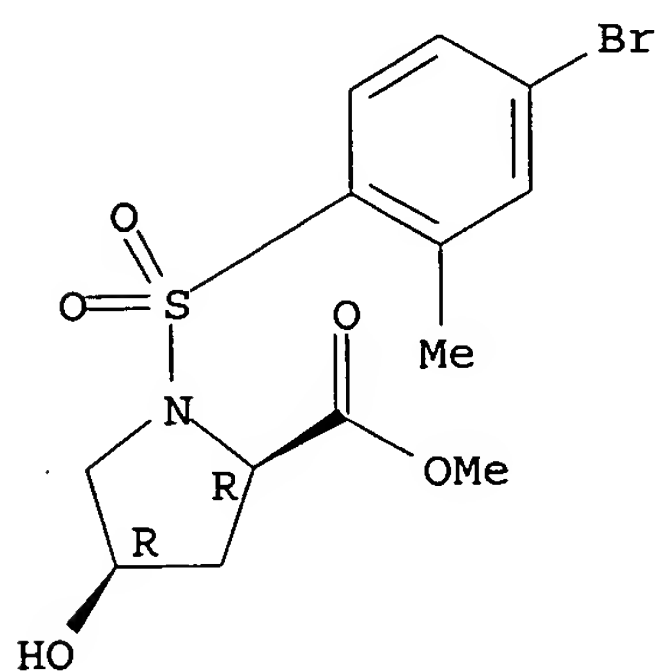
RN 204072-59-3 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxy-2-nitrophenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

(4R) - (9CI) (CA INDEX NAME)

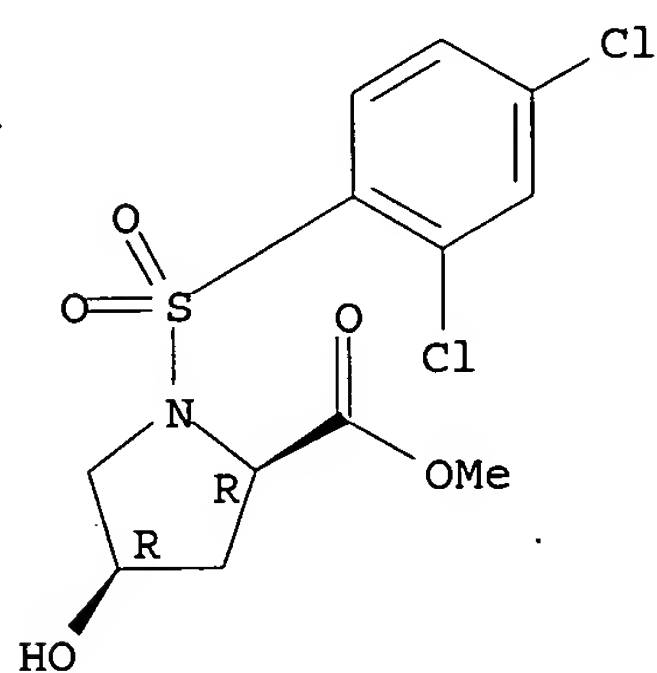
Absolute stereochemistry.



RN 204072-52-6 HCAPLUS

CN D-Proline, 1-[(2,4-dichlorophenyl)sulfonyl]-4-hydroxy-, methyl ester,  
(4R) - (9CI) (CA INDEX NAME)

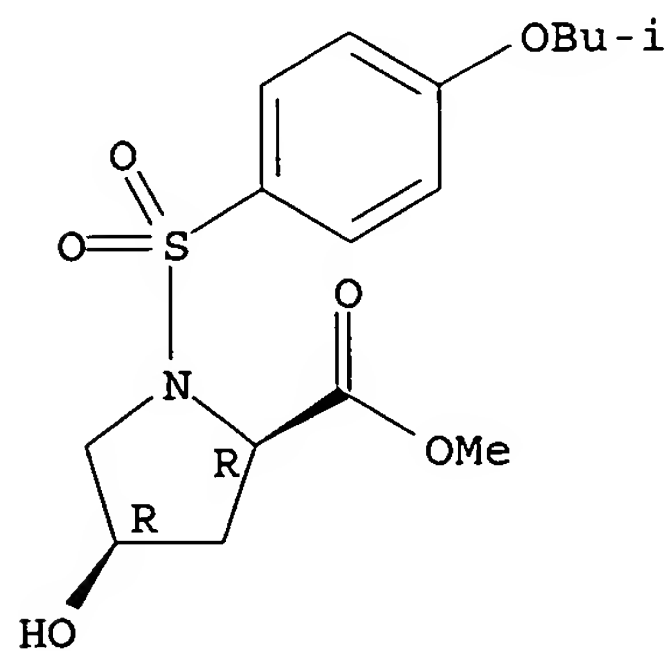
Absolute stereochemistry.

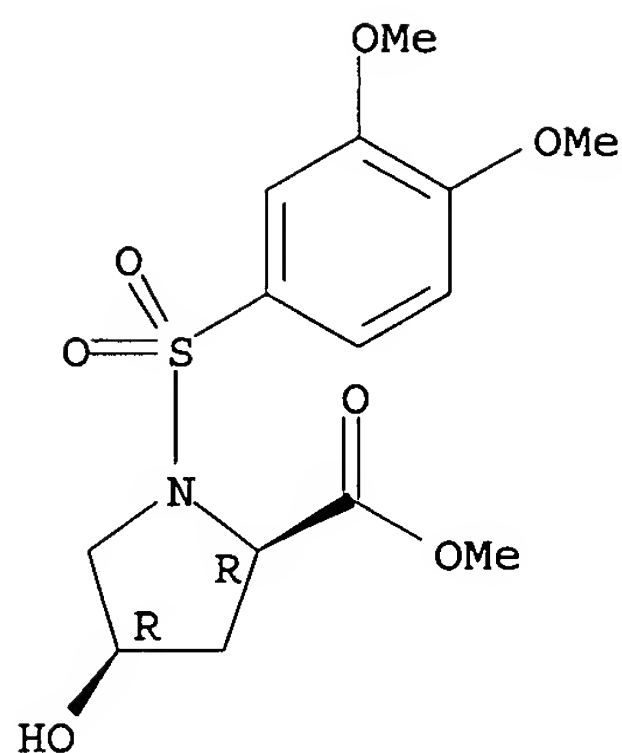


RN 204072-56-0 HCAPLUS

CN D-Proline, 4-hydroxy-1-[[4-(2-methylpropoxy)phenyl]sulfonyl]-, methyl  
ester, (4R) - (9CI) (CA INDEX NAME)

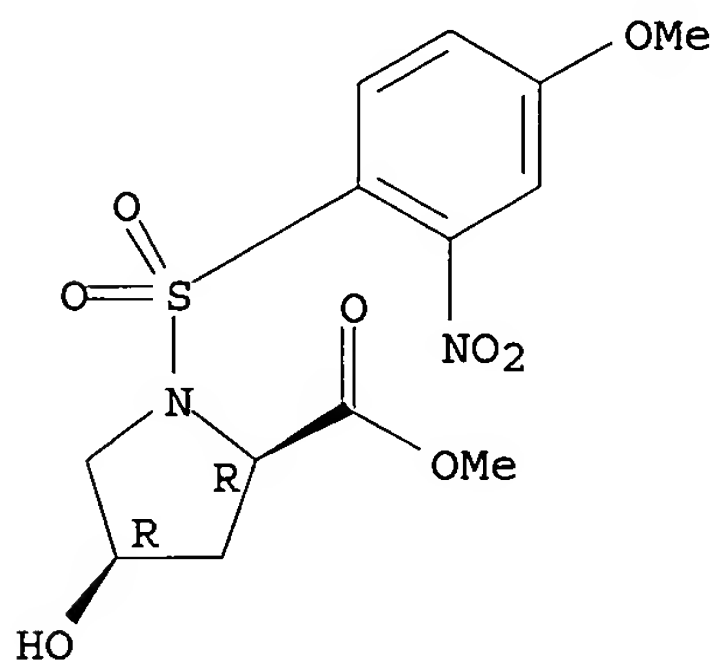
Absolute stereochemistry.





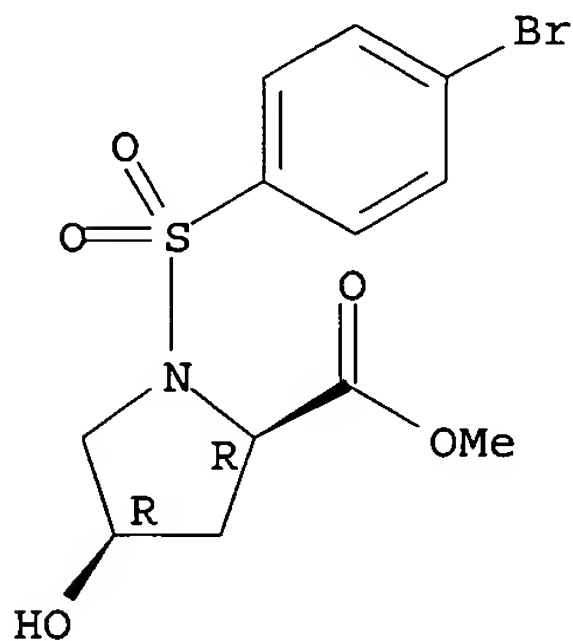
RN 204072-47-9 HCAPLUS  
 CN D-Proline, 4-hydroxy-1-[(4-methoxy-2-nitrophenyl)sulfonyl]-, methyl ester,  
 (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-50-4 HCAPLUS  
 CN D-Proline, 1-[(4-bromophenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

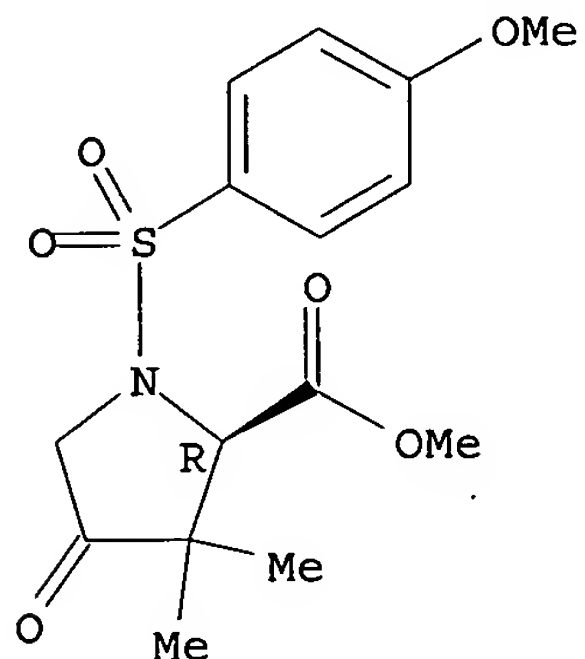


RN 204072-51-5 HCAPLUS  
 CN D-Proline, 1-[(4-bromo-2-methylphenyl)sulfonyl]-4-hydroxy-, methyl ester,

RN 204072-44-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-4-oxo-, methyl ester  
(9CI) (CA INDEX NAME)

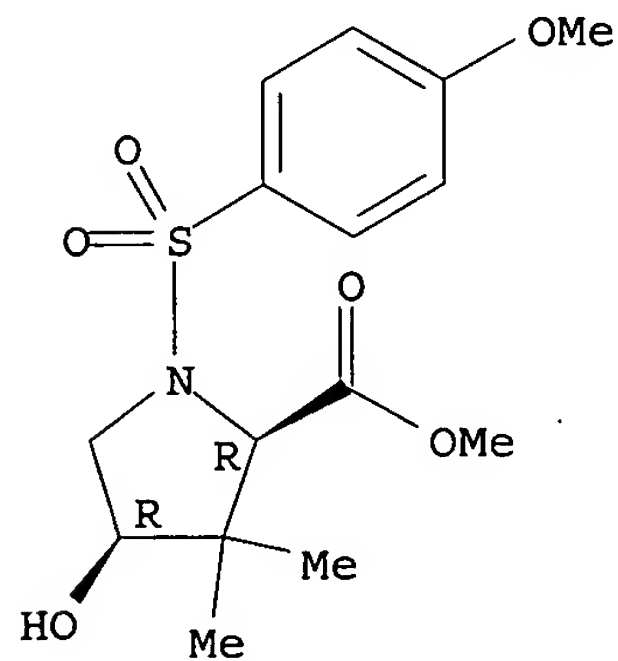
Absolute stereochemistry.



RN 204072-45-7 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



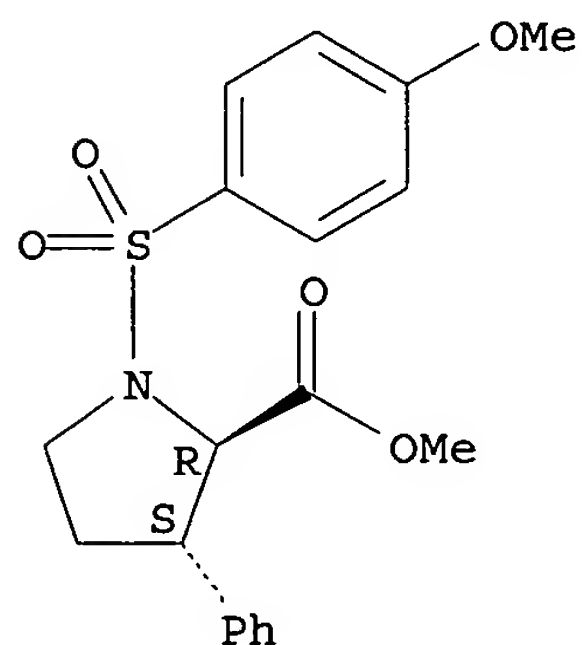
RN 204072-46-8 HCAPLUS

CN D-Proline, 1-[(3,4-dimethoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-3-phenyl-, methyl ester,  
(3S)-rel- (9CI) (CA INDEX NAME)

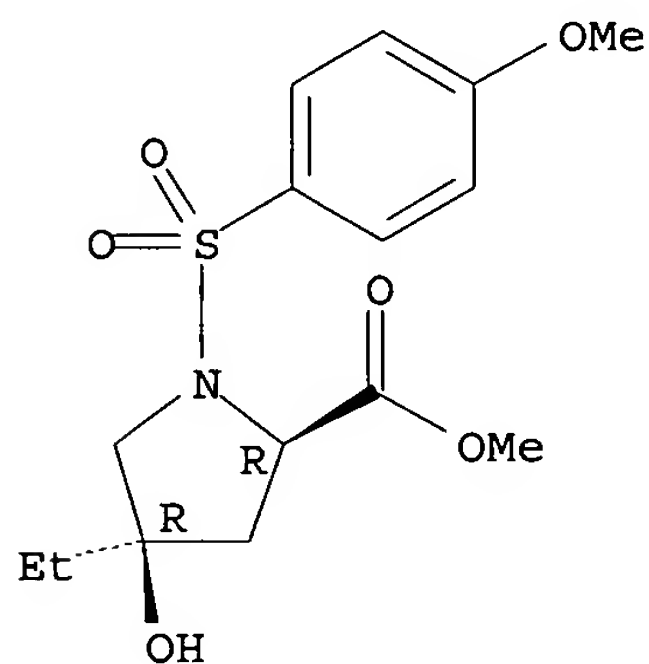
Relative stereochemistry.



RN 204072-41-3 HCAPLUS

CN D-Proline, 4-ethyl-4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester,  
(4R)- (9CI) (CA INDEX NAME)

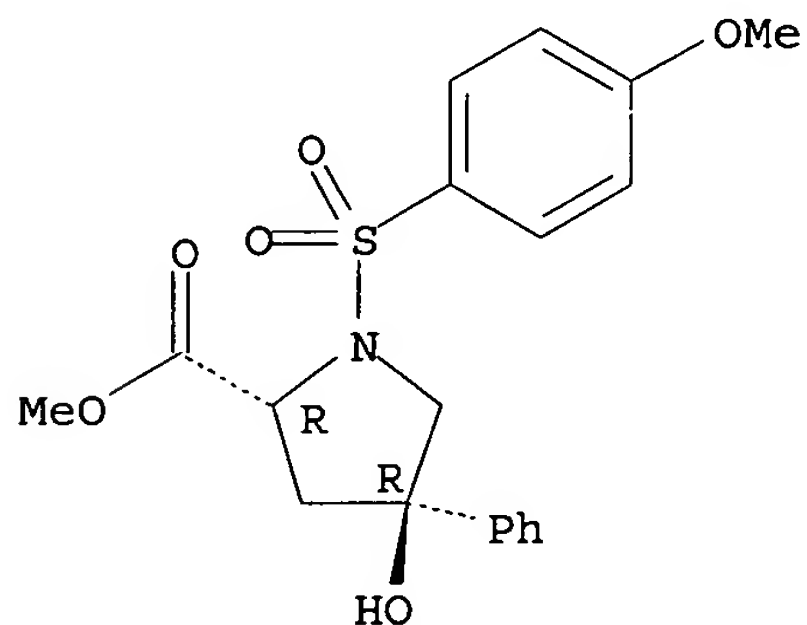
Absolute stereochemistry.



RN 204072-42-4 HCAPLUS

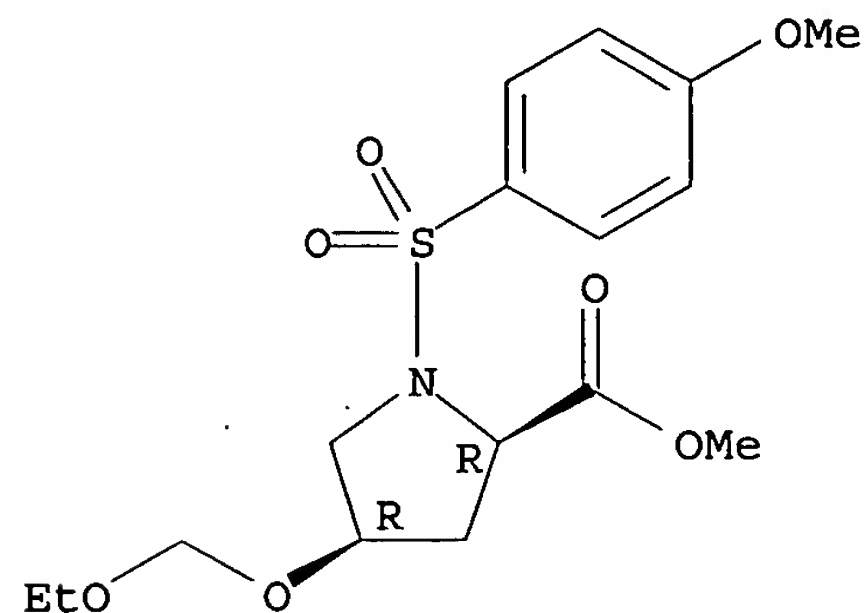
CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-phenyl-, methyl  
ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CN D-Proline, 4-(ethoxymethoxy)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester,  
(4R)- (9CI) (CA INDEX NAME)

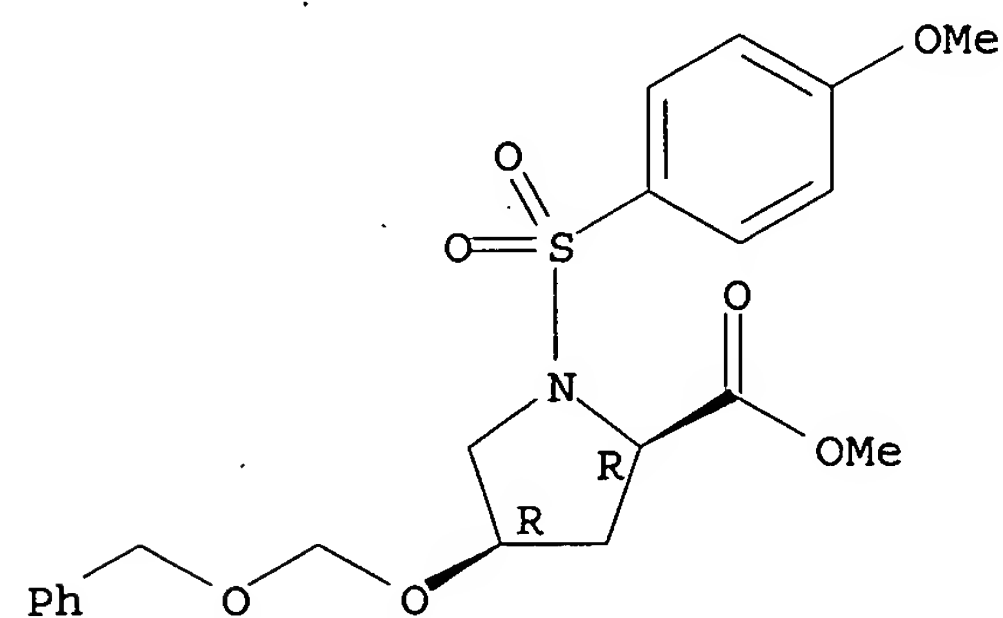
Absolute stereochemistry.



RN 204072-37-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(phenylmethoxy)methoxy]-,  
methyl ester, (4R)- (9CI) (CA INDEX NAME)

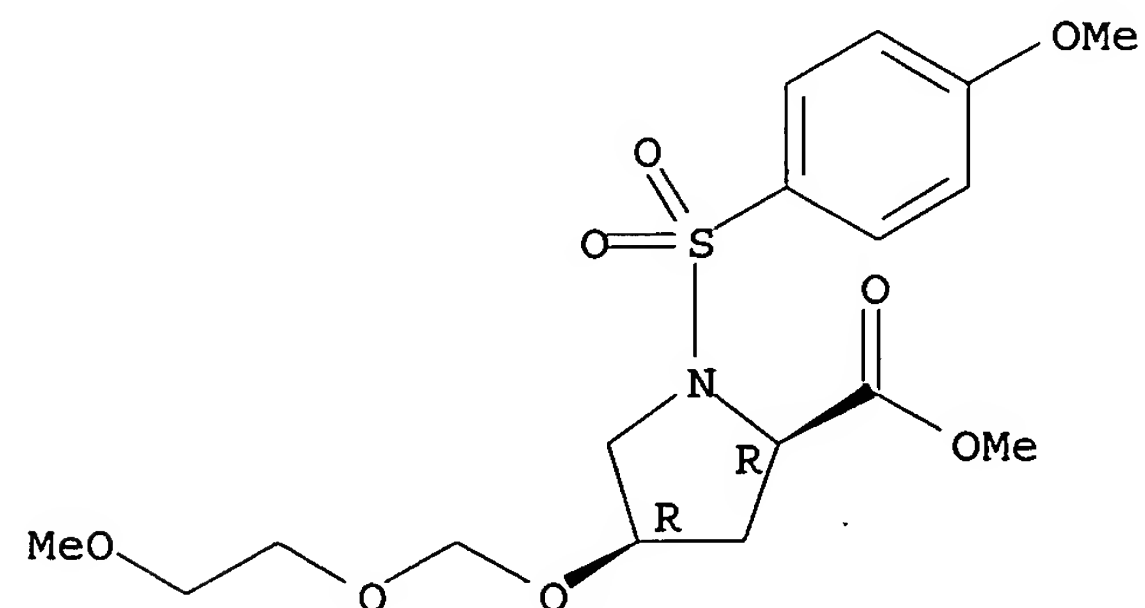
Absolute stereochemistry.



RN 204072-38-8 HCAPLUS

CN D-Proline, 4-[(2-methoxyethoxy)methoxy]-1-[(4-methoxyphenyl)sulfonyl]-,  
methyl ester, (4R)- (9CI) (CA INDEX NAME)

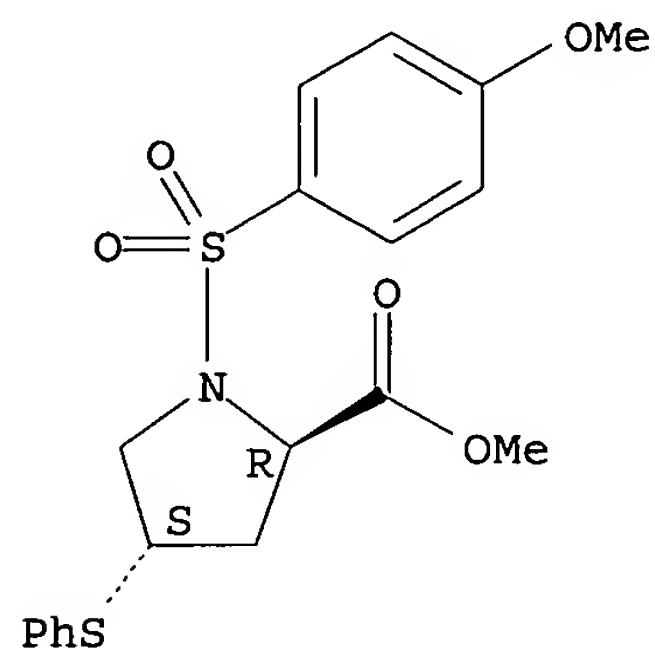
Absolute stereochemistry.



RN 204072-39-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(phenylthio)-, methyl ester,  
(4S)- (9CI) (CA INDEX NAME)

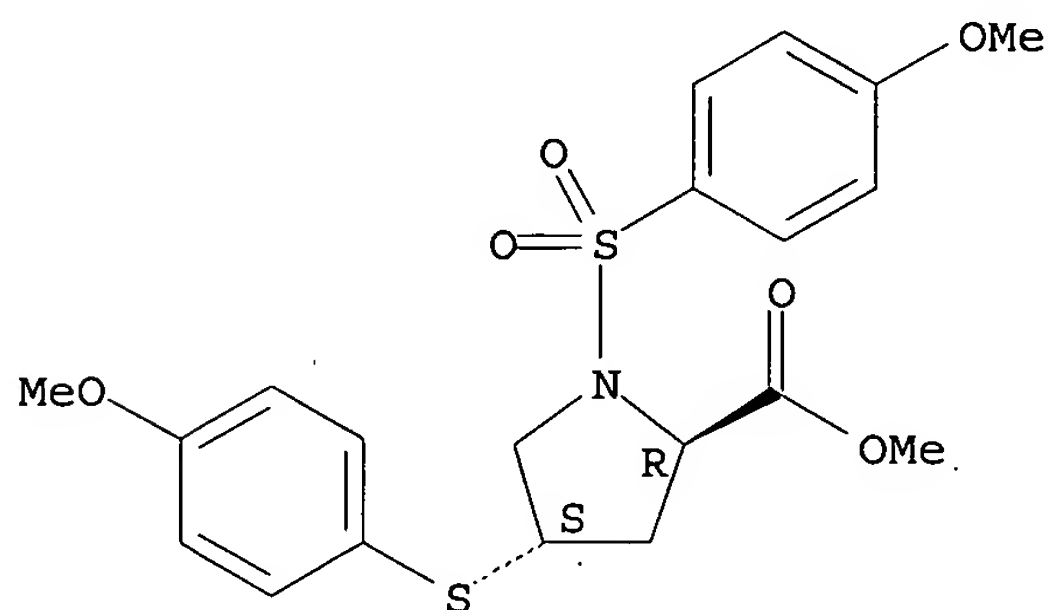
Absolute stereochemistry.



RN 204072-32-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(4-methoxyphenyl)thio]-,  
methyl ester, (4S)- (9CI) (CA INDEX NAME)

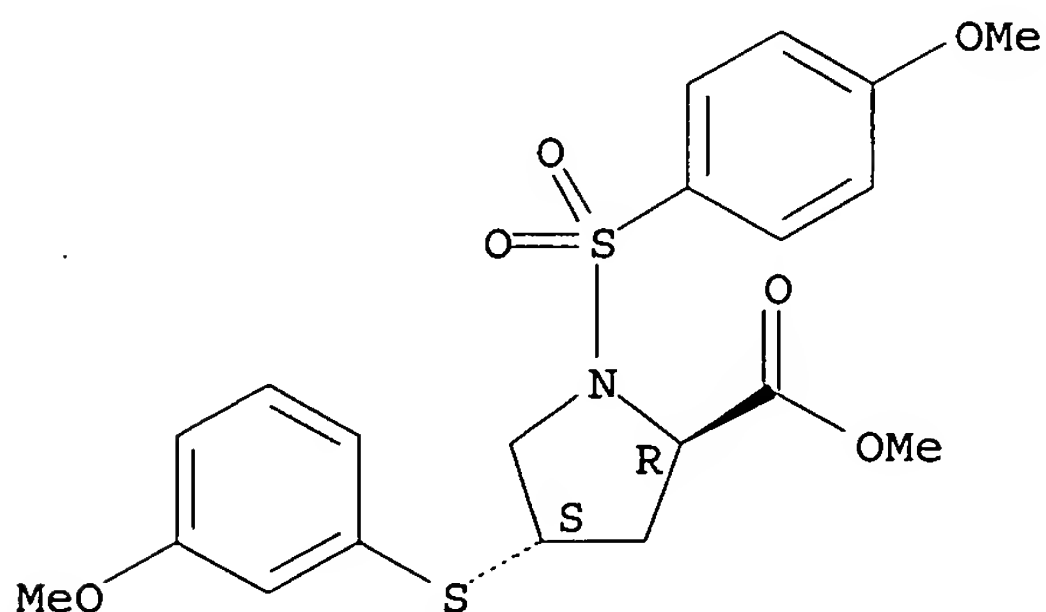
Absolute stereochemistry.



RN 204072-34-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(3-methoxyphenyl)thio]-,  
methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

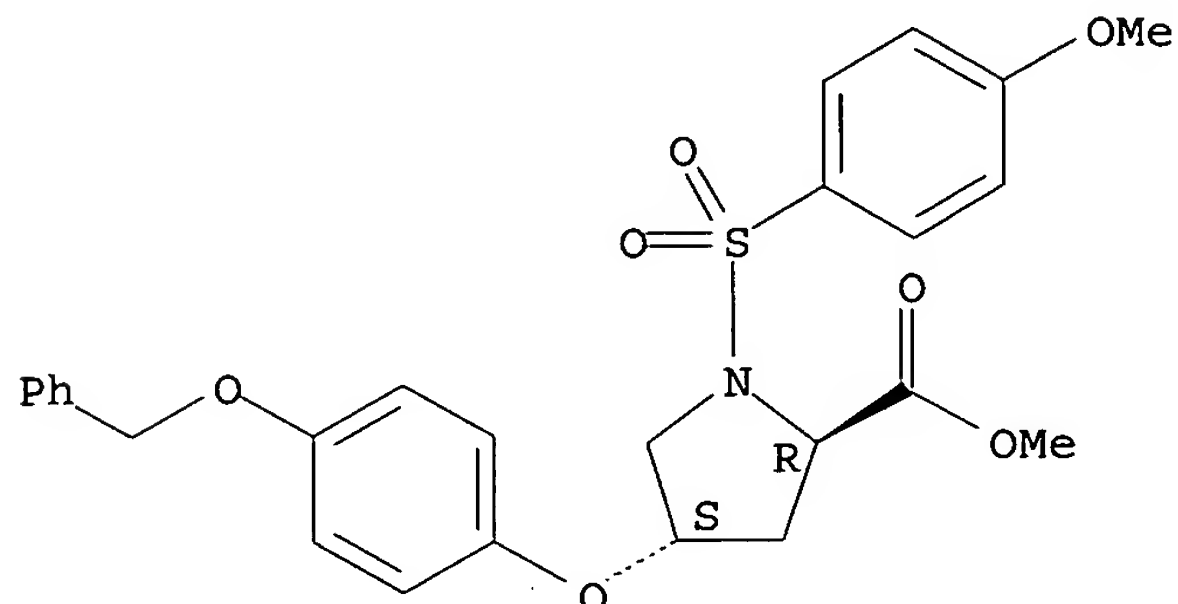


RN 204072-36-6 HCAPLUS



CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[4-(phenylmethoxy)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

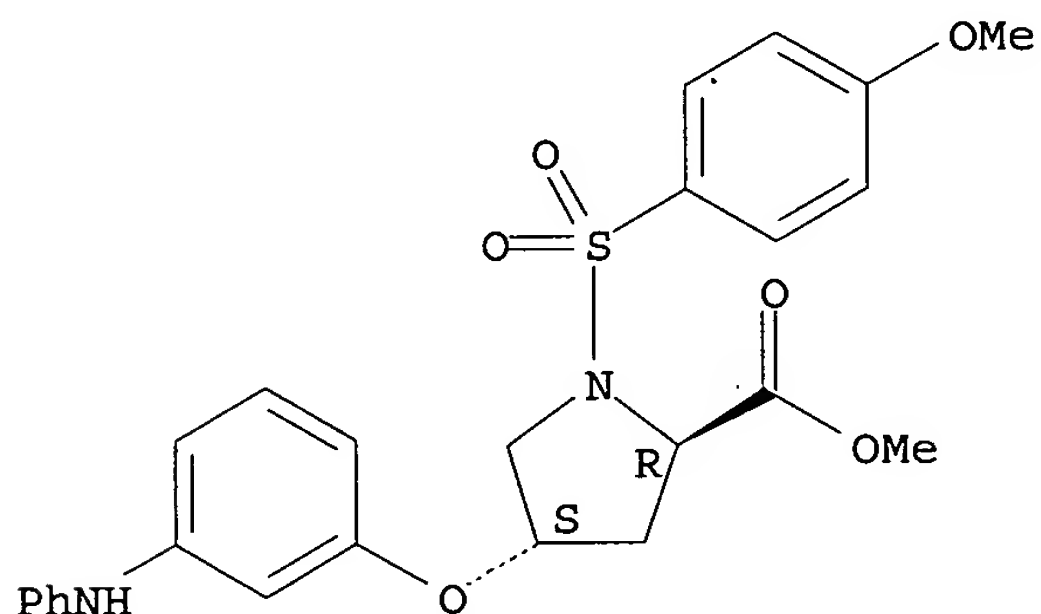
Absolute stereochemistry.



RN 204072-28-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(phenylamino)phenoxy]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

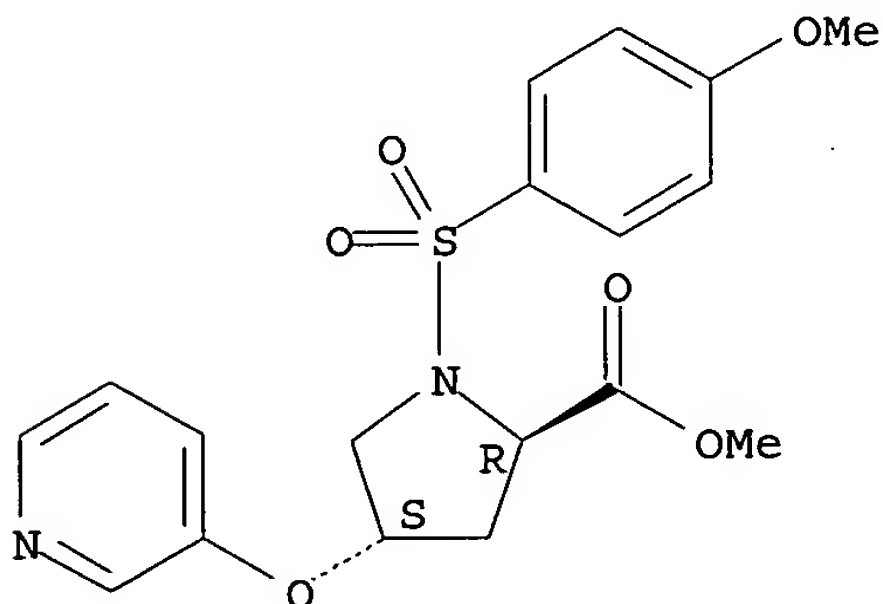
Absolute stereochemistry.



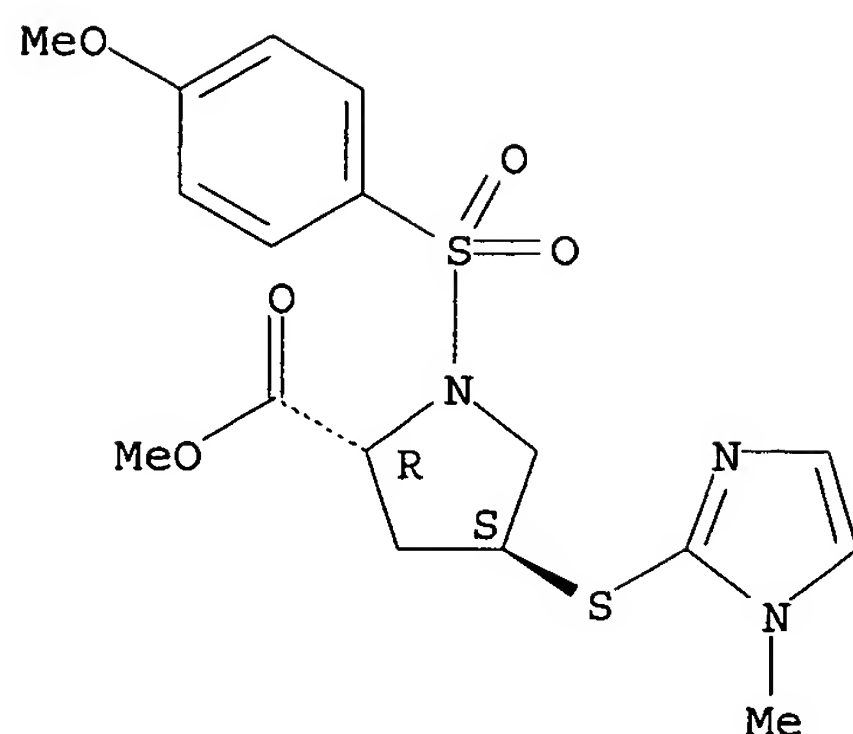
RN 204072-29-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(3-pyridinyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



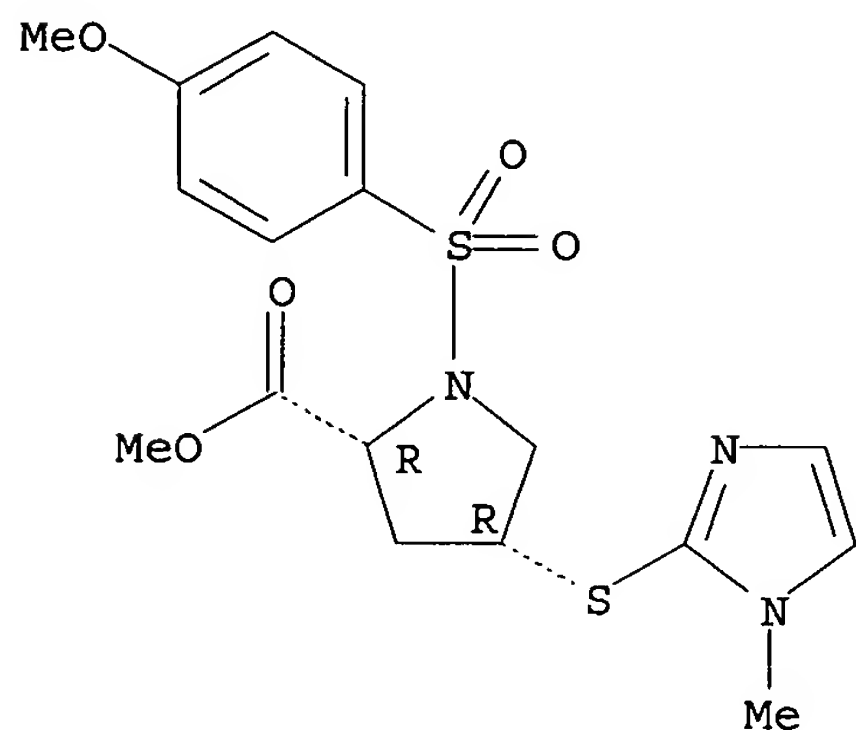
RN 204072-30-0 HCAPLUS



RN 204072-25-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-methyl-1H-imidazol-2-yl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

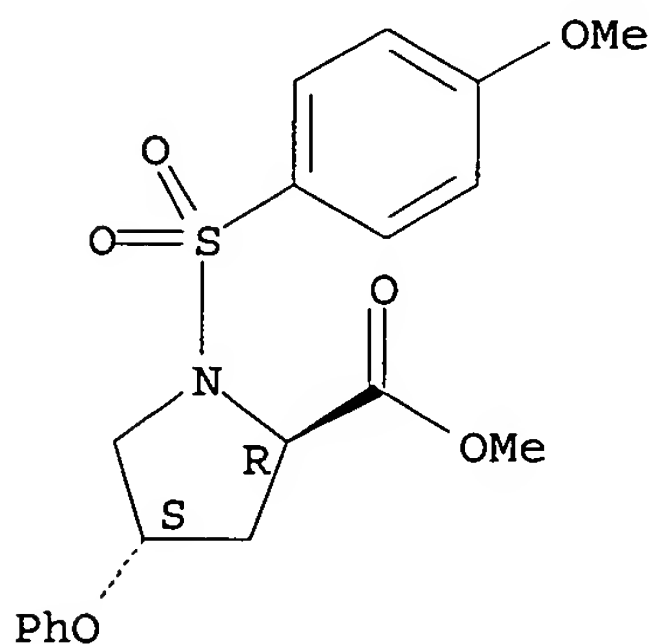
Absolute stereochemistry.



RN 204072-26-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-phenoxy-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

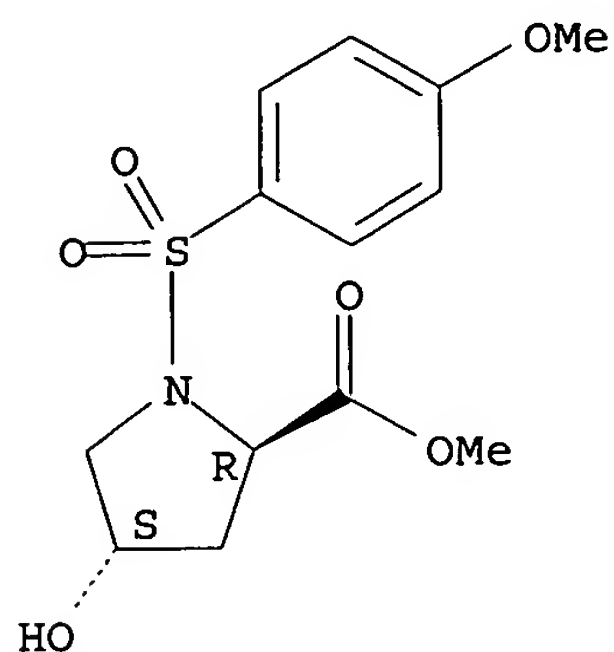
Absolute stereochemistry.



RN 204072-27-5 HCAPLUS

(9CI) (CA INDEX NAME)

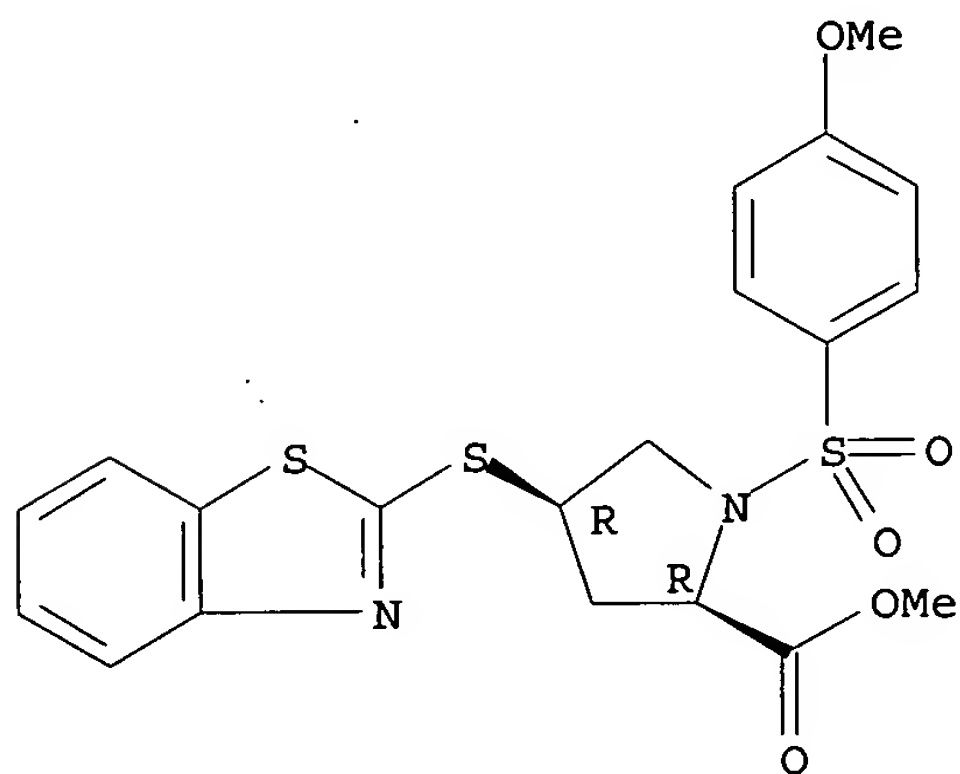
Absolute stereochemistry.



RN 204072-23-1 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

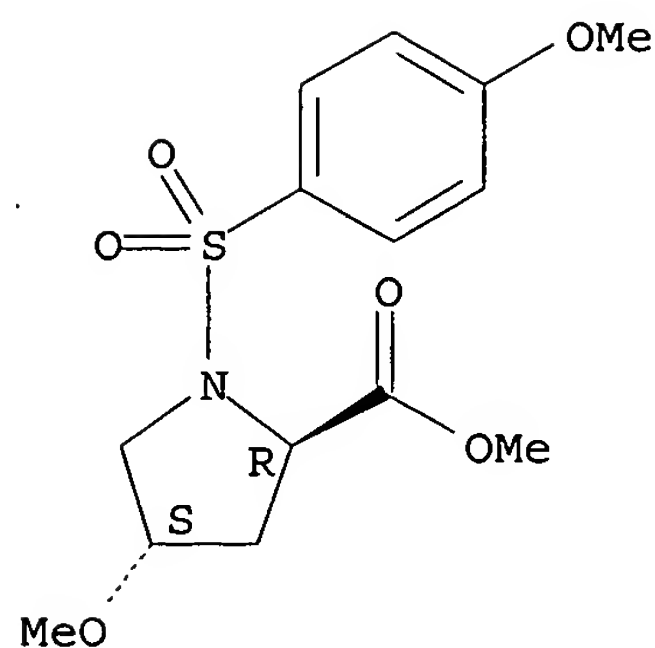
Absolute stereochemistry.



RN 204072-24-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-methyl-1H-imidazol-2-yl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

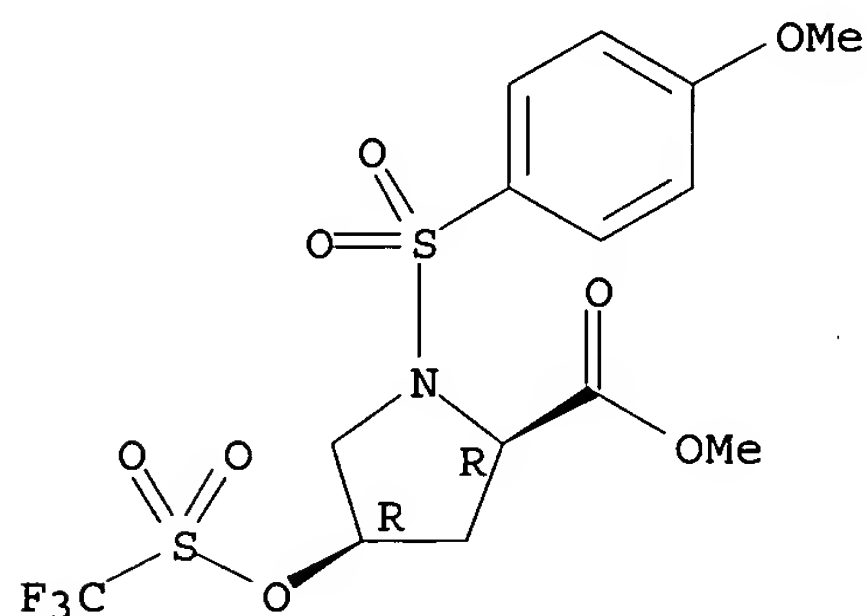
Absolute stereochemistry.



RN 204072-20-8 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[trifluoromethylsulfonyl]oxy]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

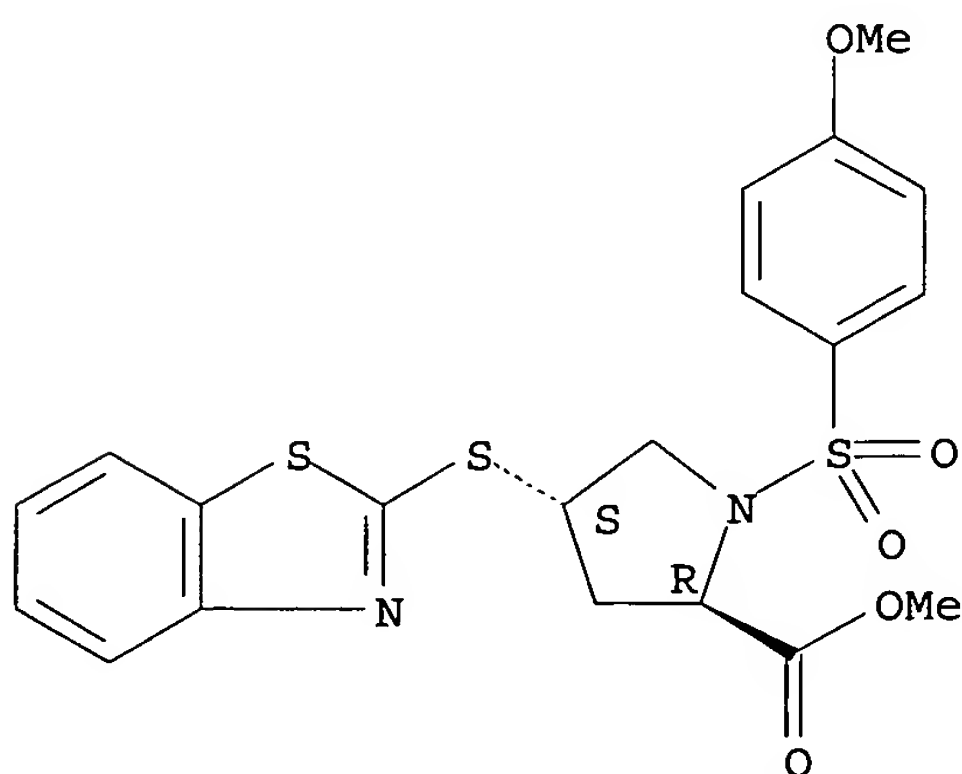
Absolute stereochemistry.



RN 204072-21-9 HCAPLUS

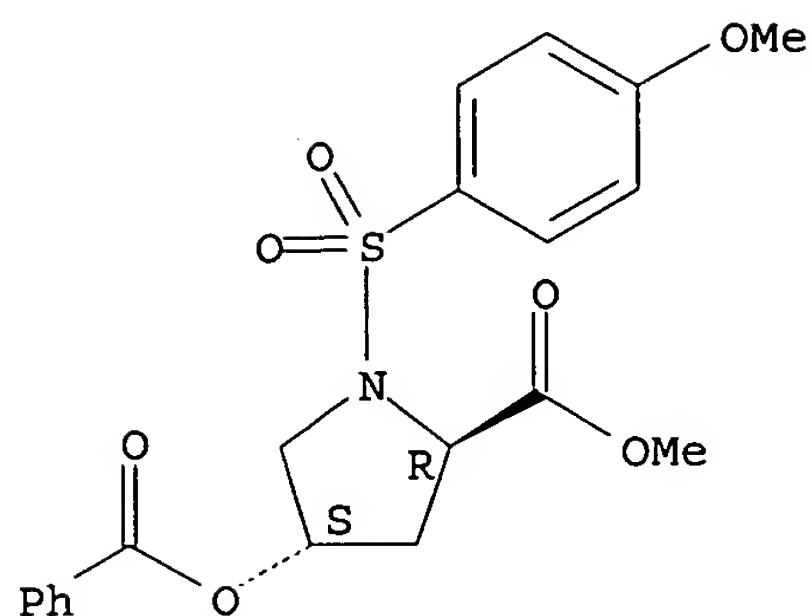
CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-22-0 HCAPLUS

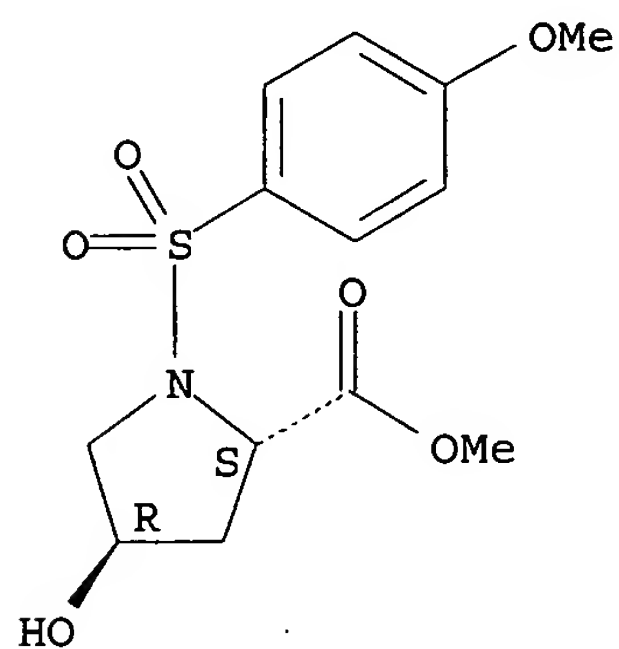
CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-



RN 204072-16-2 HCAPLUS

CN L-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)-  
(9CI) (CA INDEX NAME)

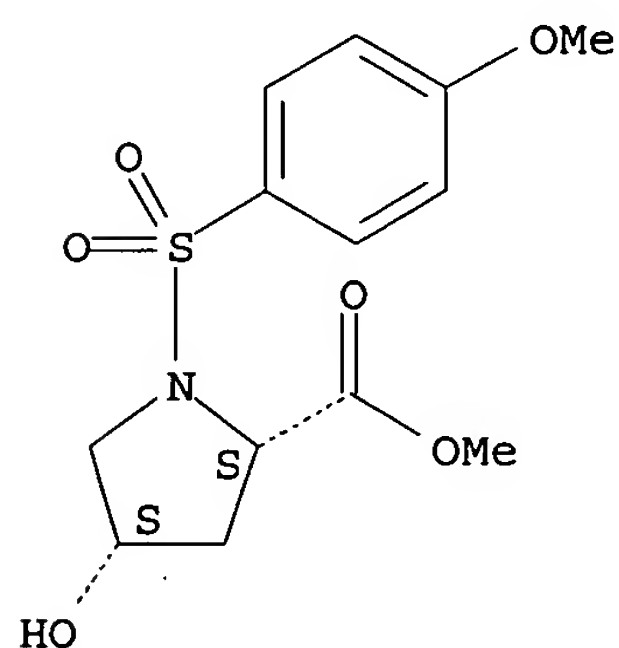
Absolute stereochemistry.



RN 204072-17-3 HCAPLUS

CN L-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

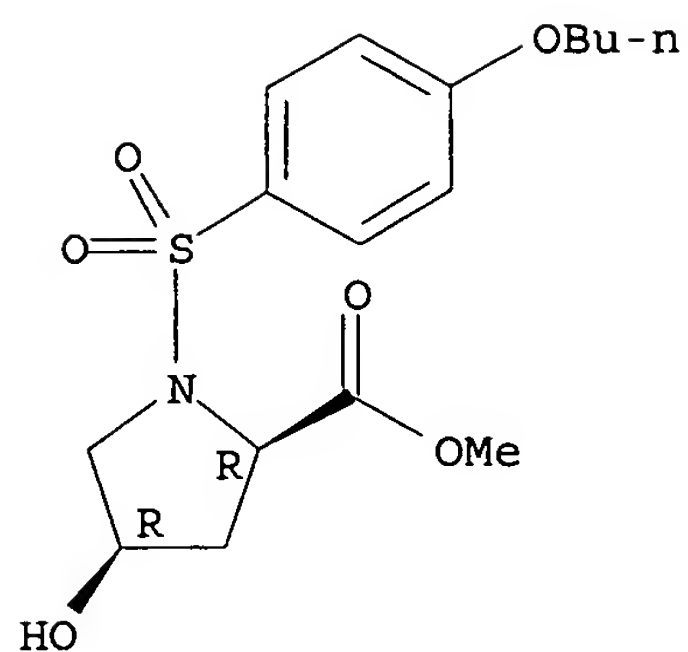
Absolute stereochemistry.



RN 204072-19-5 HCAPLUS

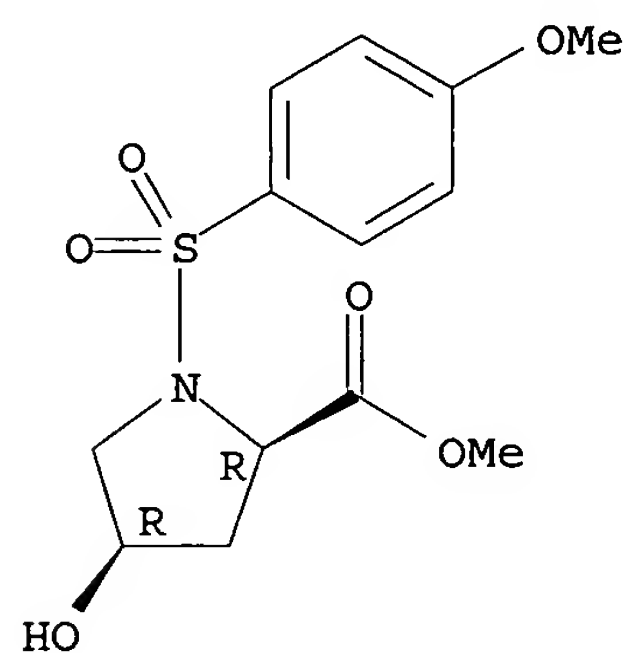
CN D-Proline, 4-methoxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



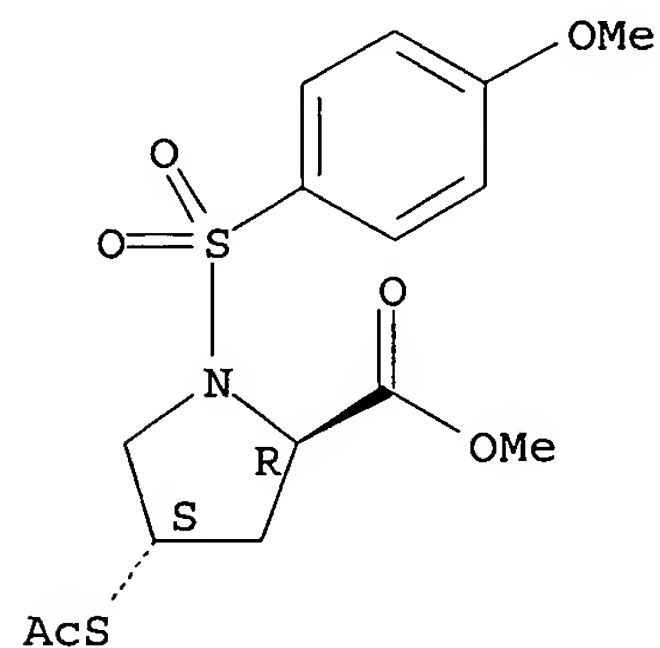
RN 203994-80-3 HCAPLUS  
 CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 203994-82-5 HCAPLUS  
 CN D-Proline, 4-(acetylthio)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-15-1 HCAPLUS  
 CN D-Proline, 4-(benzoyloxy)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

722550-49-4P, 1-[4-(2-Methoxyethyl)phenylsulfonyl]-(2R)-  
carbomethoxy-(4R)-hydroxypyrrolidine 722550-52-9P,

1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-5-pyrrolidinone

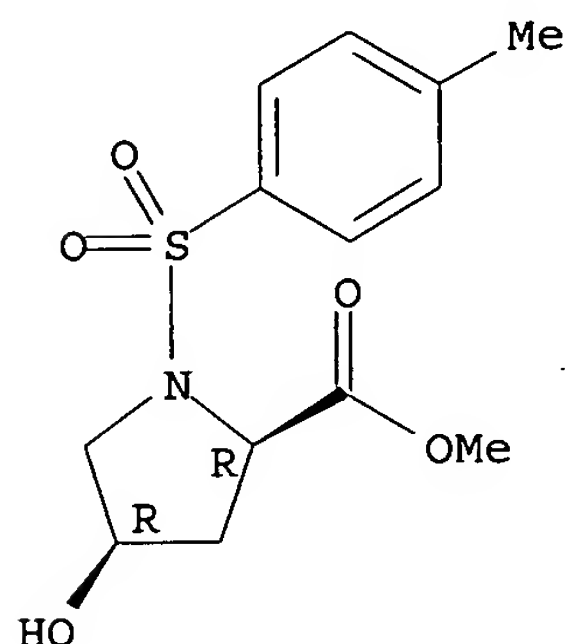
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(intermediate; preparation of N-sulfonyl pyrrolidine-2-carbohydroxamic acid  
as metalloprotease inhibitors for treatment of restenosis)

RN 57850-07-4 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-methylphenyl)sulfonyl]-, methyl ester, (4R)-  
(9CI) (CA INDEX NAME)

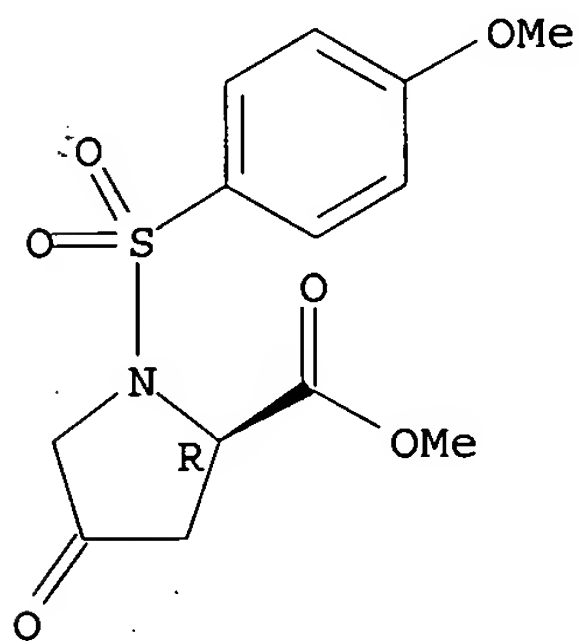
Absolute stereochemistry.



RN 203934-42-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



RN 203934-63-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

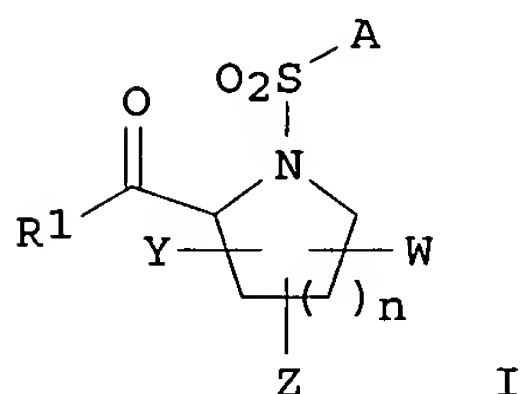
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US 2003105153	A1	20030605	US 2002-186531	20020701 <--
US 6872742	B2	20050329		
US 2003191163	A1	20031009	US 2002-308780	20021203 <--
US 6858628	B2	20050222		
JP 2004115531	A2	20040415	JP 2003-384116	20031113
US 2005101567	A1	20050512	US 2004-3594	20041203
PRIORITY APPLN. INFO.:			US 1996-24842P	P 19960828
			US 1997-918317	A3 19970826
			US 2001-888675	A2 20010625
			US 2001-888759	B2 20010625
			US 2002-186531	A2 20020701
			JP 1998-511715	A3 19970822
			US 2002-308780	A3 20021203

OTHER SOURCE(S): MARPAT 141:123901  
GI



AB The invention provides compds. according to formula (I), in particular N-sulfonylpyrrolidine-2-carboxylic acid derivs., [wherein A = each (un)substituted alkyl, heteroalkyl, aryl, or heteroaryl; R1 = NHOR2 (where R2 = H, alkyl); W = one or more of H, lower alkyl, or an alkylene bridge that forms a ring in addition to the main ring; Y = independently one or more of HO, SR3, SOR4, SO2R8, alkoxy, or (un)substituted amino (where R8 = alkyl, aryl, heteroaryl, heteroalkyl, amino, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino); Z = H, HO, or alkyl, or an alkylene or heteroalkylene bridge that forms a ring in addition to the main ring; n = 1; some provisos applied], pharmaceutically-acceptable salts, biohydrolyzable amides, esters, or imides thereof are prepared These compds. are useful as **inhibitors** of metalloproteases, and effective in treating conditions characterized by excess activity of these **enzymes**, in particular restenosis. Thus, cis-hydroxy-D-propine was condensed with 4-methylphenylsulfonyl chloride in the presence of Et3N and 2,6-dimethylpyridine in aqueous dioxane at room temperature for 14 h gave N-(4-methylphenylsulfonyl)-cis-hydroxy-D-propine which was esterified with MeOH and SOCl2 to give N-(4-methylphenylsulfonyl)-cis-hydroxy-D-propine Me ester which was treated with hydroxylamine monopotassium salt in MeOH overnight to give (2R,4S)-1-(4-Methoxyphenylsulfonyl)-2-(N-hydroxycarboxamido)-4S-hydroxypyrrolidine.

IT **57850-07-4P**, 1-(4-Methylphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine **203934-42-3P**, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-4-oxopyrrolidine **203934-63-8P**, 1-(4-Butoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine **203994-80-3P**, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4R)-hydroxypyrrolidine **203994-82-5P**, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-acetylthiopyrrolidine **204072-15-1P**, 1-(4-Methoxyphenylsulfonyl)-(2R)-carbomethoxy-(4S)-benzoyloxypyrrolidine

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,  
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US 2002-380761P P 20020514  
 US 2002-392782P P 20020628  
 US 2002-422933P P 20021031  
 US 2002-428033P P 20021120  
 WO 2003-US15343 A2 20030514

OTHER SOURCE(S): MARPAT 141:218994

AB Administering an ED of a tTGase inhibitor to a celiac sprue or dermatitis herpetiformis patient reduces the toxic effects of toxic gluten oligopeptides, thereby attenuating or eliminating the damaging effects of gluten. Preparation and tissue transglutaminase-inhibiting activity of dihydroisoxazole moiety-containing compds. is included.

IT 220509-86-4P

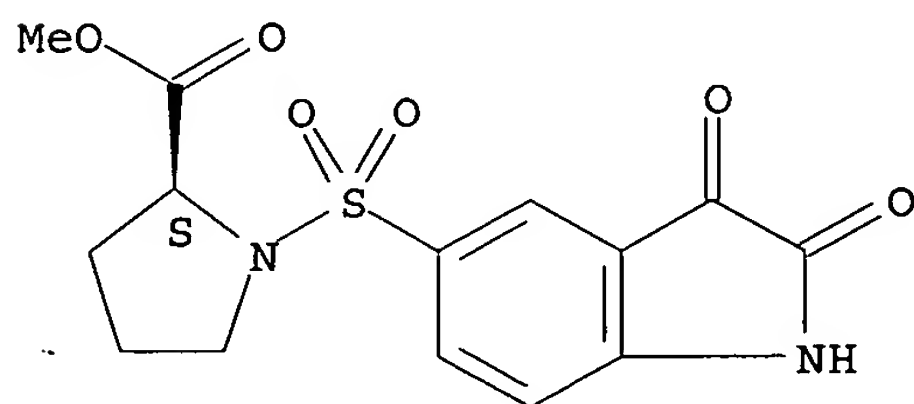
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tissue transglutaminase inhibitor therapy for celiac sprue and dermatitis herpetiformis)

RN 220509-86-4 HCAPLUS

CN L-Proline, 1-[(2,3-dihydro-2,3-dioxo-1H-indol-5-yl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L32 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:569862 HCAPLUS

DOCUMENT NUMBER: 141:123901

TITLE: Preparation of N-sulfonyl-cyclic amine-2-carbohydroxamic acid derivatives as metalloprotease inhibitors

INVENTOR(S): Natchus, Michael George; De, Biswanath; Pikul, Stanislaw; Almstead, Neil Gregory; Bookland, Roger Gunnard; Taiwo, Yetunde Olabisi; Cheng, Menyan

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 186,531.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138260	A1	20040715	US 2003-730572	20031208
US 6417219	B1	20020709	US 1997-918317	19970826 <--
US 2002061877	A1	20020523	US 2001-888675	20010625 <--
US 6569855	B2	20030527		

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L32 ANSWER 1 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:703116 HCAPLUS

DOCUMENT NUMBER: 141:218994

TITLE: Tissue transglutaminase (tTGase) inhibitor therapy for celiac sprue and dermatitis herpetiformis

INVENTOR(S): Khosla, Chaitan; Choi, Kihang

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of Appl. No. PCT/US03/15343.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

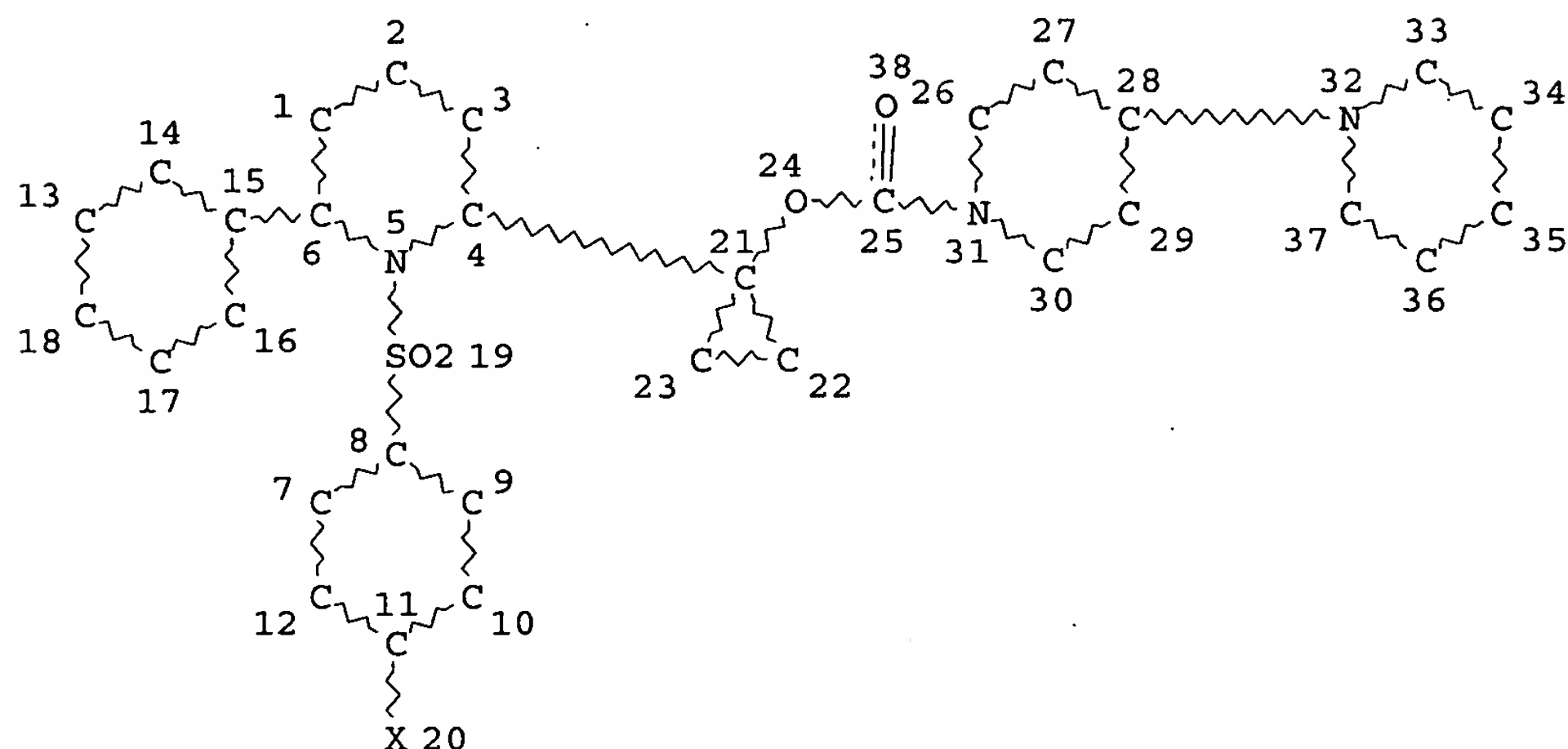
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US 2004167069	A1	20040826	US 2003-716846	20031118
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WO 2003096979	A2	20031127	WO 2003-US15343	20030514 <--
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 DEFAULT ECLEVEL IS LIMITED

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STEREO ATTRIBUTES: NONE  
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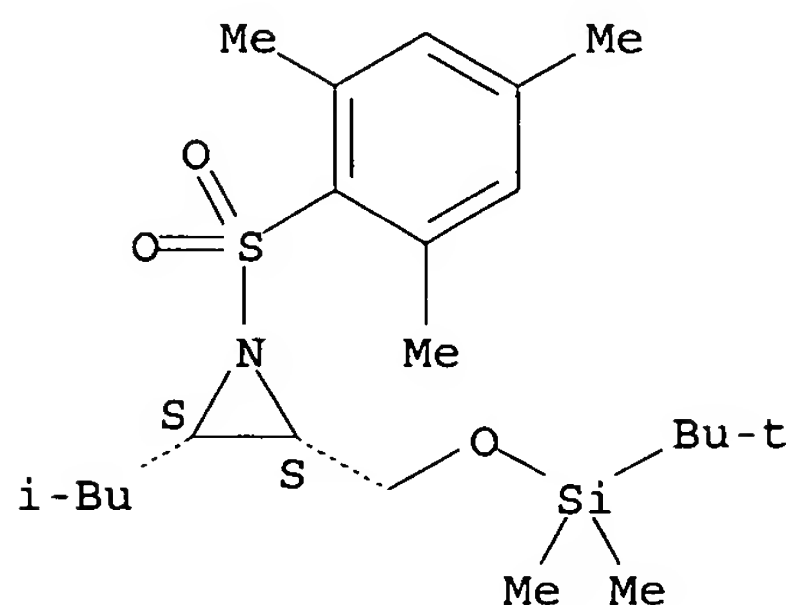
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 DEFAULT ECLEVEL IS LIMITED

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 L18 183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE  
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Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L4 STR

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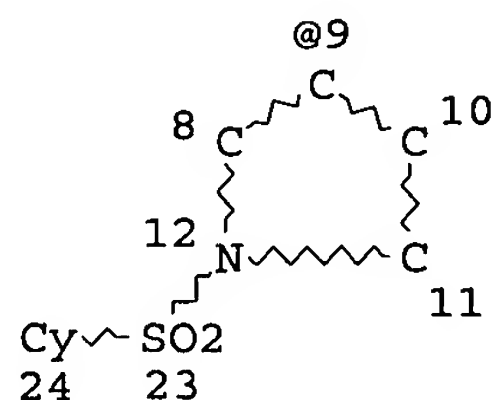
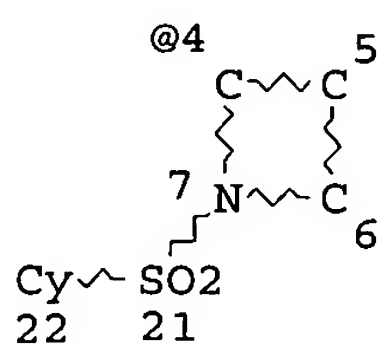
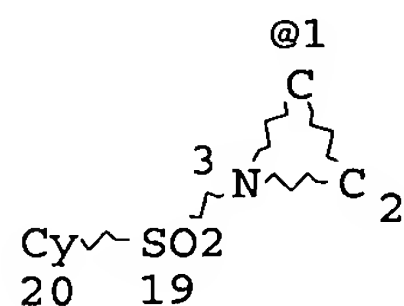
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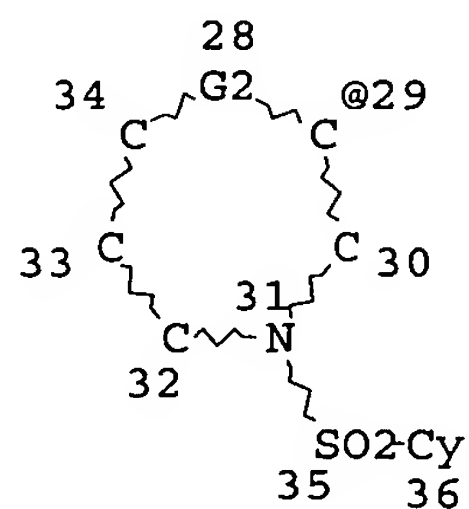
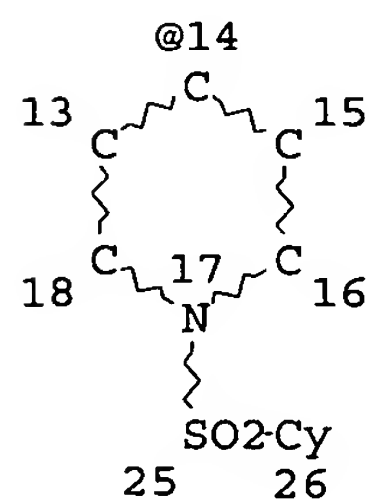
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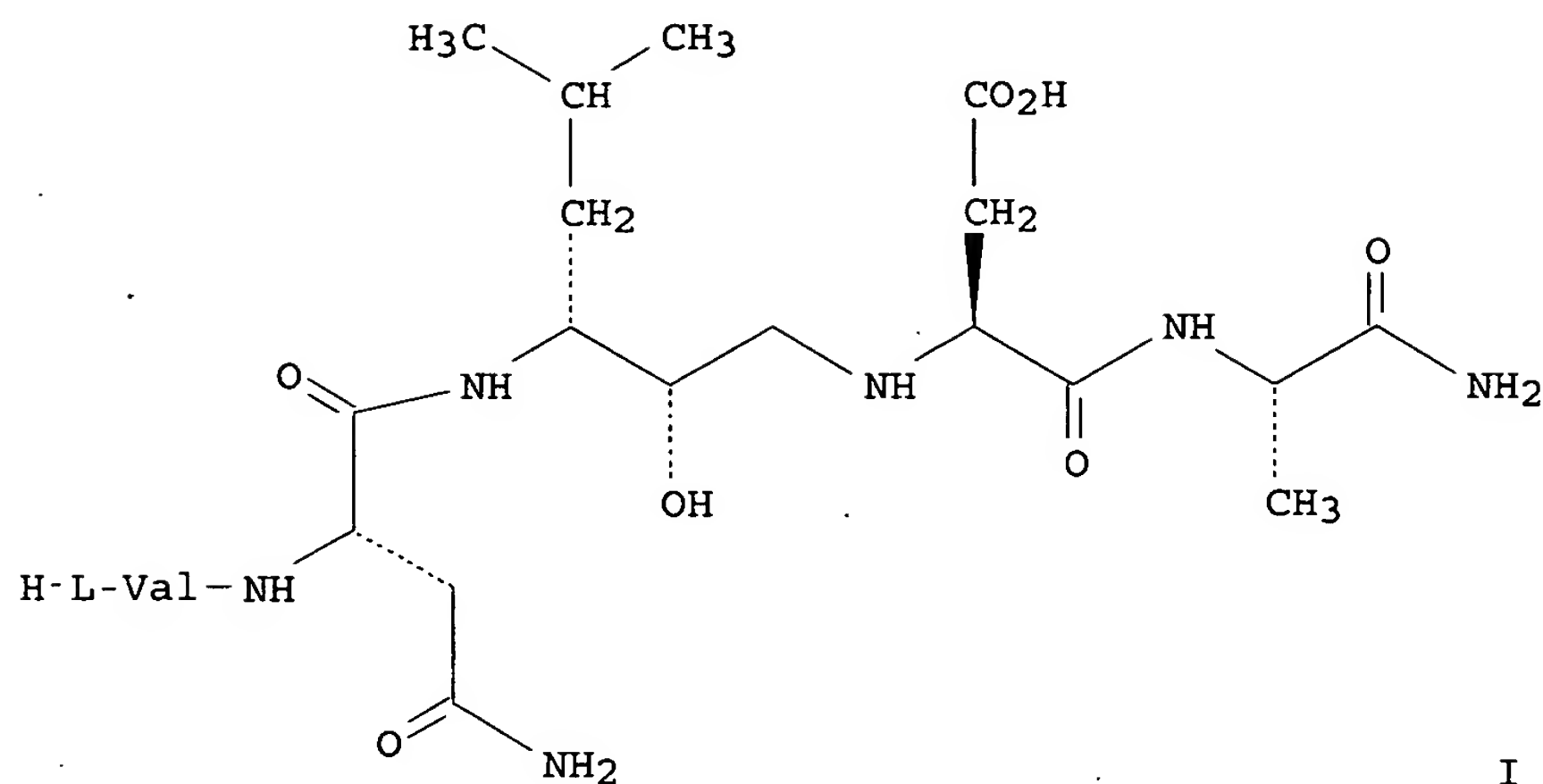
STEREO ATTRIBUTES: NONE

L10 STR



G1 27





AB A novel methodol. utilizing the aza-Payne rearrangement and O, N-intramol. acyl transfer reactions for the synthesis of peptidomimetics containing hydroxyethylamine dipeptide isosteres (HDIs) (e.g., I) is described. This methodol. is useful for the stereoselective synthesis of HDI-containing pseudopeptides, and applicable to combinatorial chemical using solid-phase techniques.

IT 433922-90-8P 433922-91-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

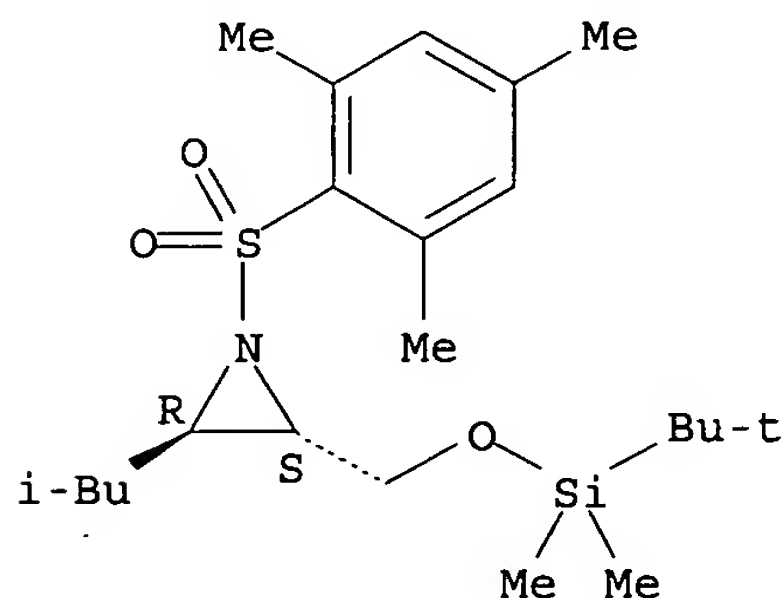
(preparation of hydroxyethylamine dipeptide isostere-containing peptidomimetics

as potential  $\beta$ -secretase inhibitors using aza-Payne rearrangement)

RN 433922-90-8 HCAPLUS

CN Aziridine, 2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-(2-methylpropyl)-1-[(2,4,6-trimethylphenyl)sulfonyl]-, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 433922-91-9 HCAPLUS

CN Aziridine, 2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-(2-methylpropyl)-1-[(2,4,6-trimethylphenyl)sulfonyl]-, (2S,3S)- (9CI) (CA INDEX NAME)



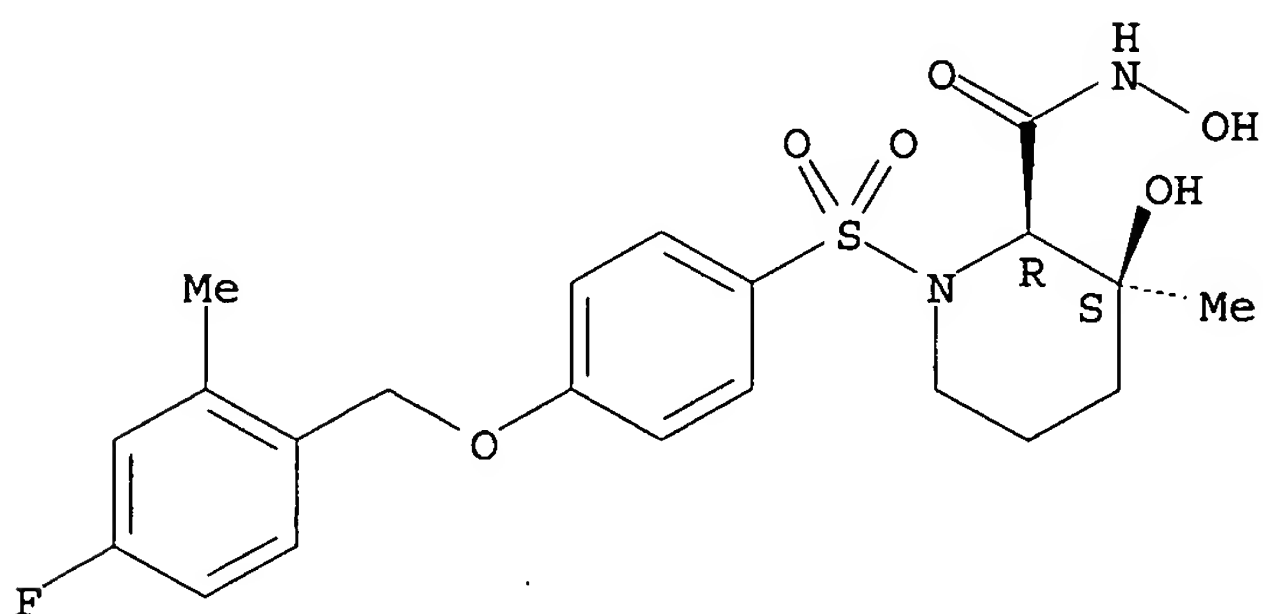
(Biological study); USES (Uses)

(TACE and metalloprotease inhibitor CP-661,631 prevents amyloid precursor protein secretion but does not increase amyloid  $\beta$  levels)

RN 530135-92-3 HCAPLUS

CN 2-Piperidinecarboxamide, 1-[[4-[(4-fluoro-2-methylphenyl)methoxy]phenyl]sulfonyl]-N,3-dihydroxy-3-methyl-, (2R,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:288617 HCAPLUS

DOCUMENT NUMBER: 137:20588

TITLE: Efficient stereoselective synthesis of peptidomimetics containing hydroxyethylamine dipeptide isosteres utilizing the aza-Payne rearrangement and O, N-acyl transfer reactions

AUTHOR(S): Tamamura, Hirokazu; Hori, Tadakazu; Otaka, Akira; Fujii, Nobutaka

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan

SOURCE: Journal of the Chemical Society, Perkin Transactions 1 (2002), (5), 577-580

CODEN: JCSPCE; ISSN: 1472-7781

PUBLISHER: Royal Society of Chemistry

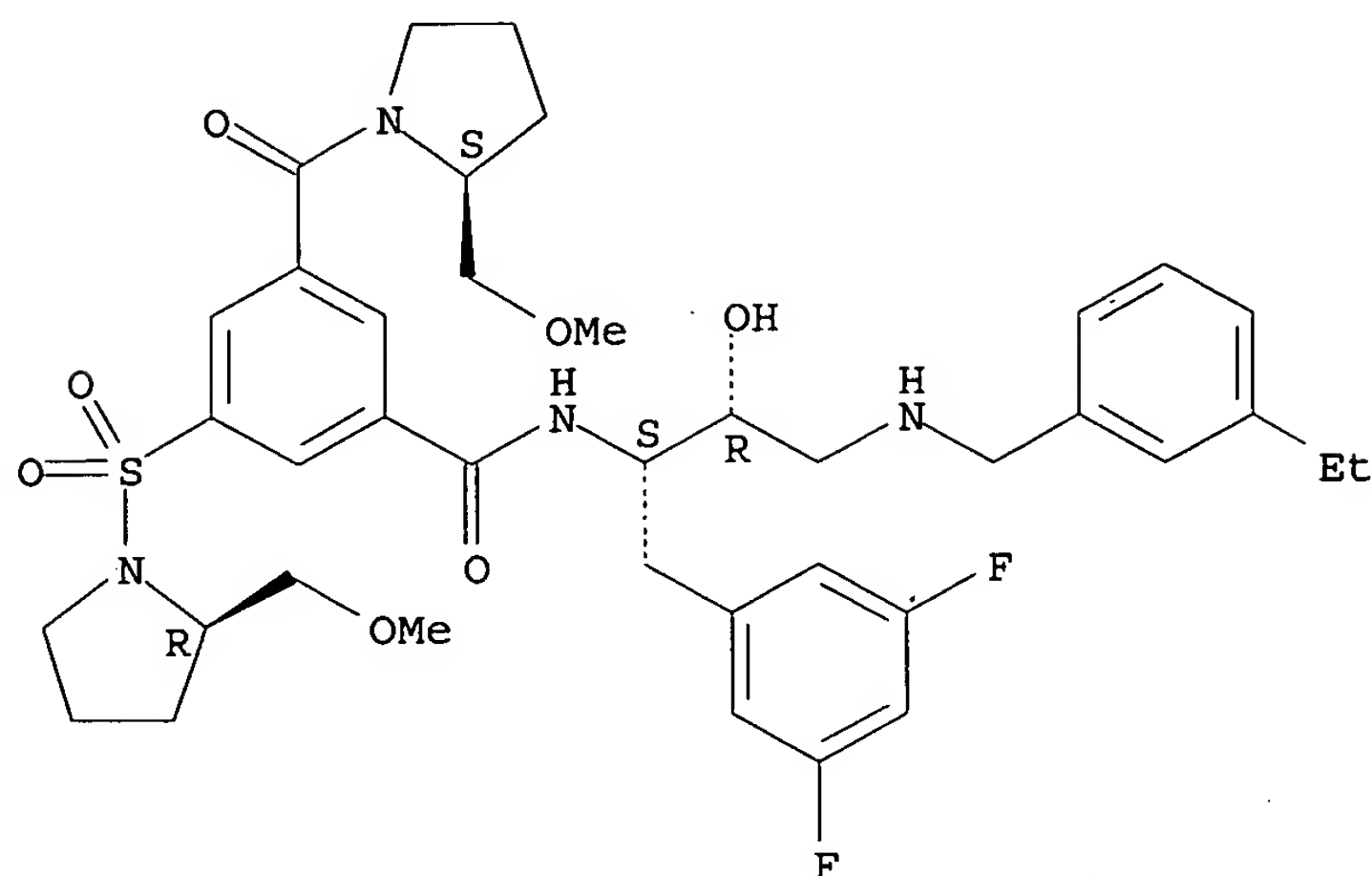
DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:20588

GI





L22 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:3568 HCAPLUS

DOCUMENT NUMBER: 138:396061

TITLE: Effect of tumor necrosis factor- $\alpha$  converting enzyme (TACE) and metalloprotease inhibitor on amyloid precursor protein metabolism in human neurons

AUTHOR(S): Blacker, Megan; Noe, Mark C.; Carty, Thomas J.; Goodyer, Cynthia G.; LeBlanc, Andrea C.

CORPORATE SOURCE: The Bloomfield Center for Research in Aging, Lady Davis Institute for Medical Research, Montreal, QC, Can.

SOURCE: Journal of Neurochemistry (2002), 83(6), 1349-1357  
CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Blackwell Science Ltd.

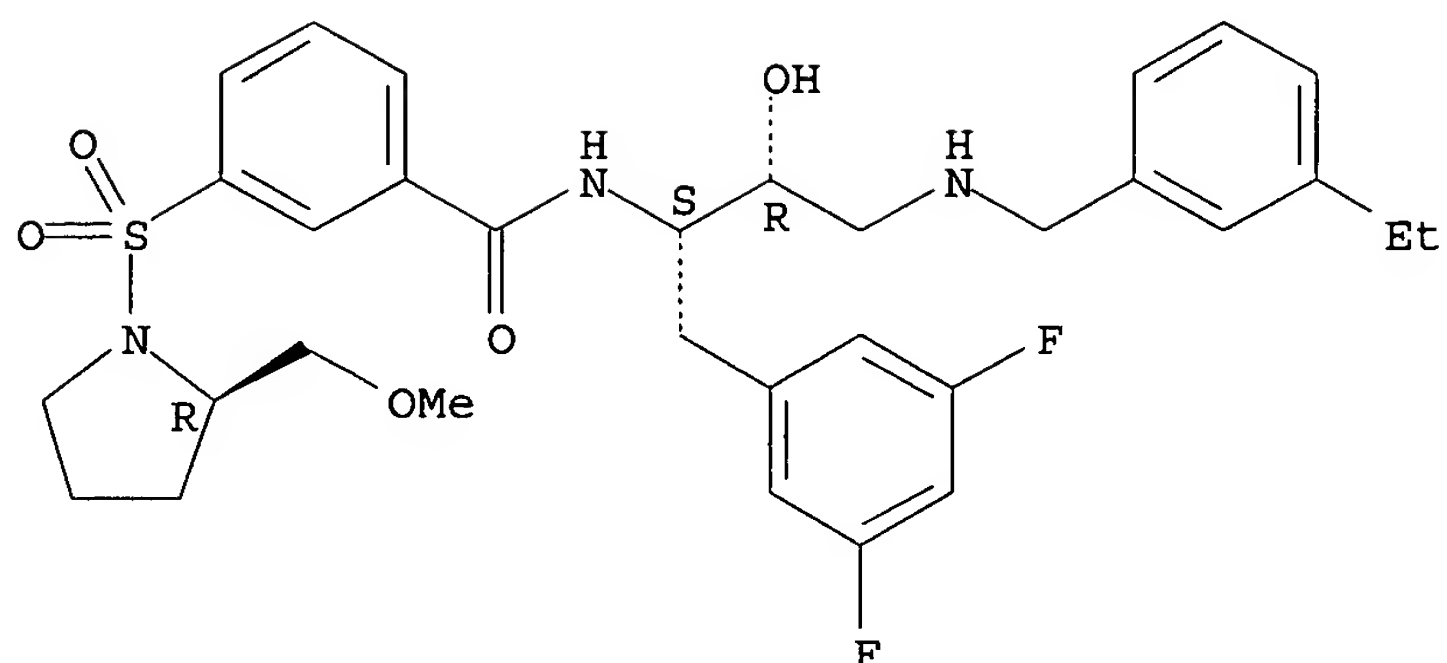
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) is implicated in inflammatory processes and much effort is being directed at inhibiting the release of TNF- $\alpha$  for treatment of inflammatory conditions. In this context, the drug CP-661,631 has been developed to inhibit the TNF- $\alpha$  converting enzyme (TACE). However, TACE is also implicated in amyloid precursor protein secretion. Amyloid precursor protein (APP) undergoes constitutive and regulated secretion by  $\alpha$ -secretase endoproteolytic cleavage within the amyloid  $\beta$  peptide (A $\beta$ ) domain. Alternative cleavage at the N- and C-terminus of the A $\beta$  domain by  $\beta$ - and  $\gamma$ -secretases results in the production of A $\beta$ . In many cellular and in vivo animal models, increased secretion of APP results in a concomitant decrease in the production of A $\beta$  suggesting that the two pathways are intricately linked. However, in human primary neuron cultures, increased APP secretion is not associated with a decrease in total A $\beta$  production. To determine if the use of CP-661,631 may enhance amyloidogenic processing in human brain, we have assessed the effect of CP-661,631 on APP metabolism in primary cultures of human neurons. Our results show that CP-661,631 effectively prevents regulated APP secretion but does not increase total A $\beta$  levels in human primary neuron cultures.

IT 530135-92-3, CP 661631

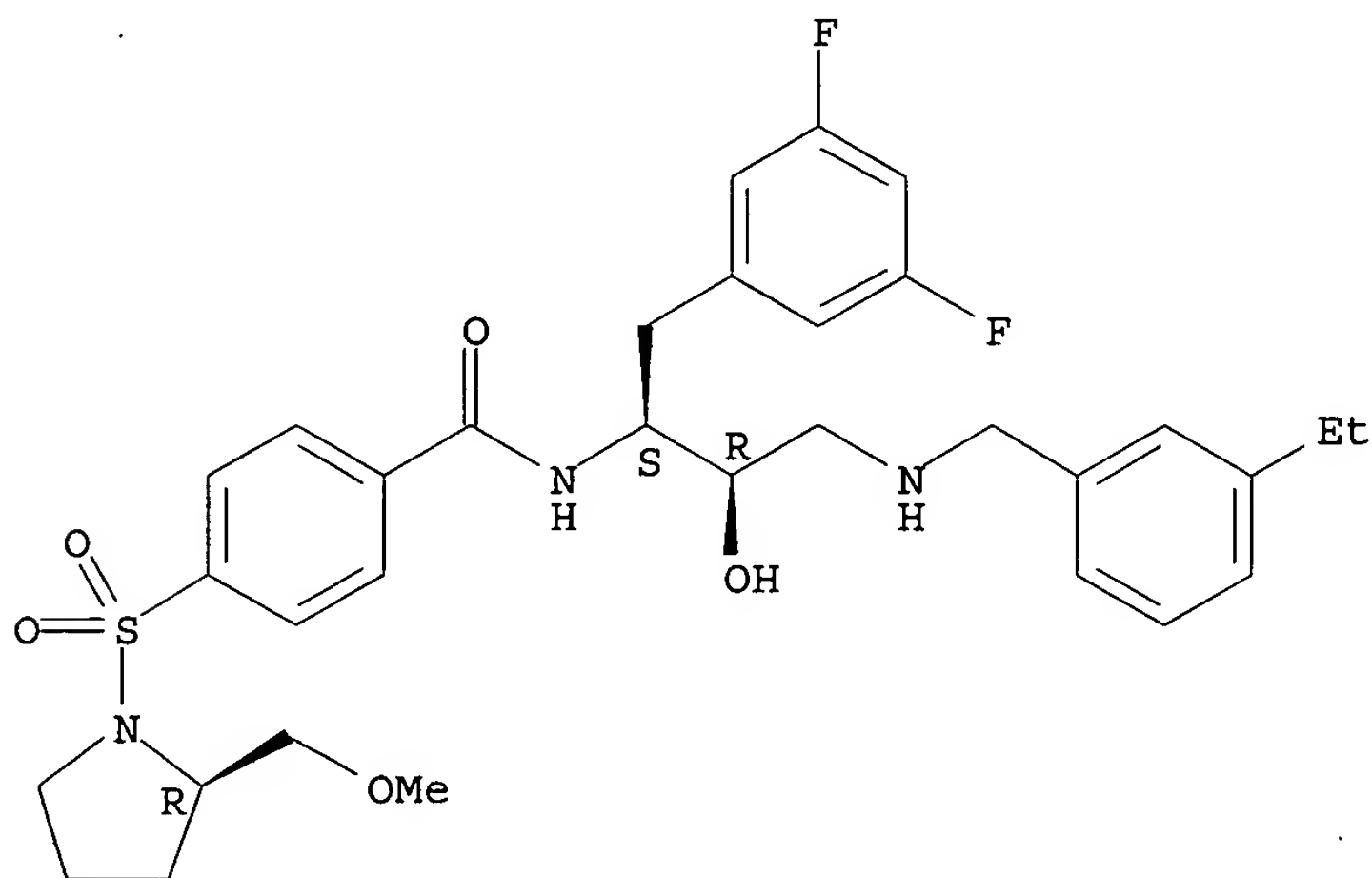
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL



RN 527728-27-4 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-4-[[2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

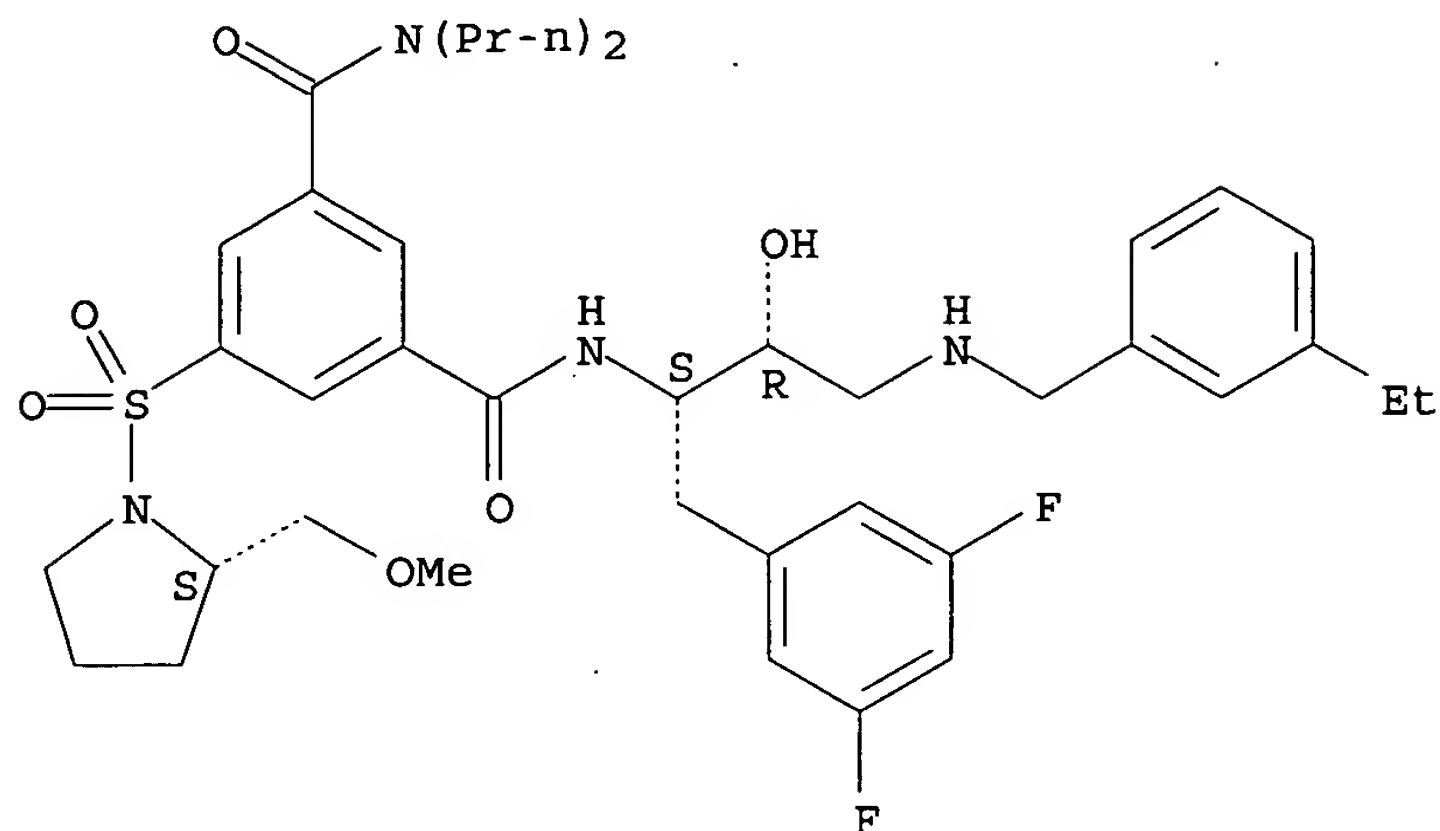


RN 527728-83-2 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-3-[[2S)-2-(methoxymethyl)-1-pyrrolidinyl]carbonyl]-5-[[2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

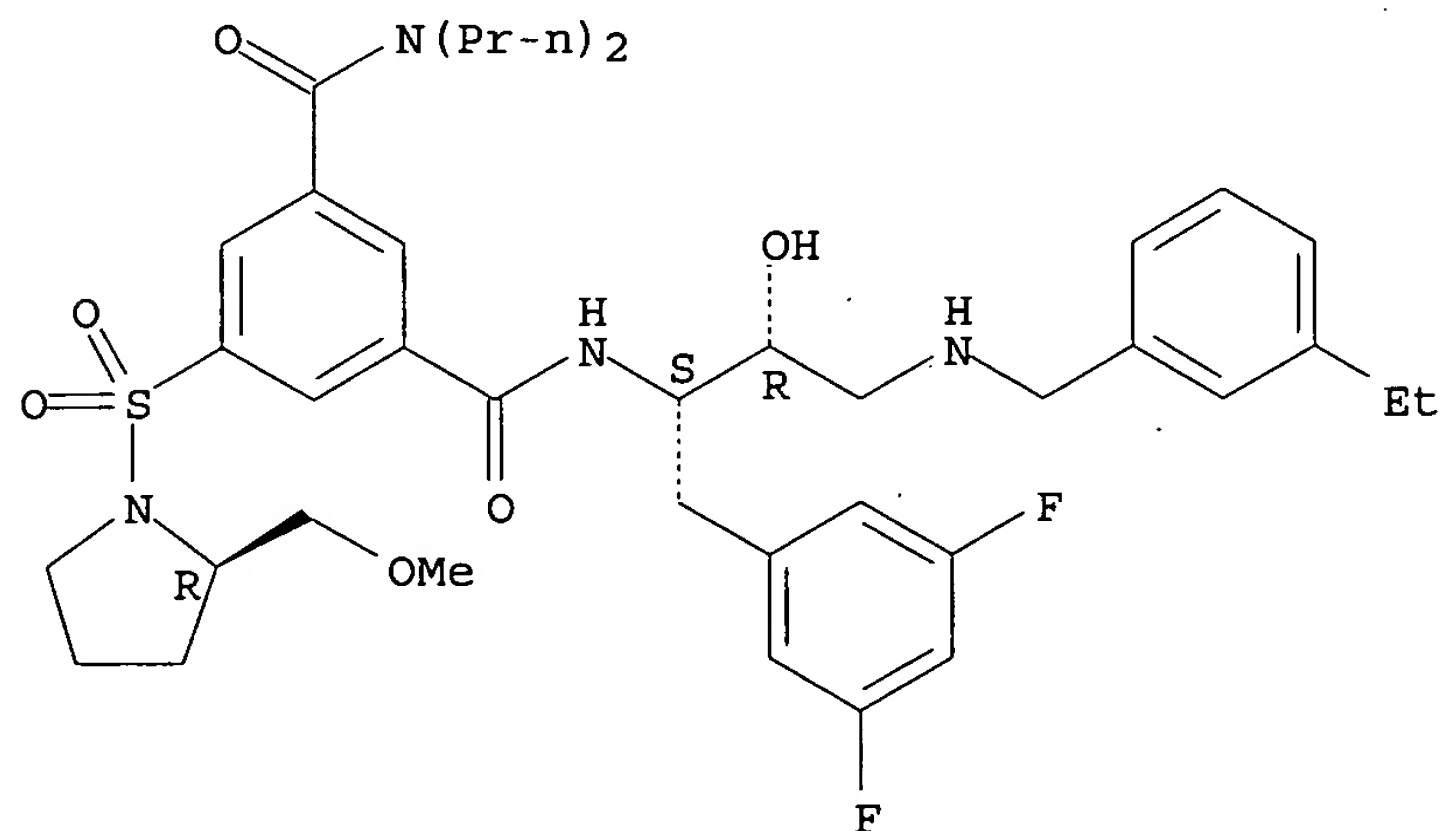
Absolute stereochemistry.



RN 527726-39-2 HCAPLUS

CN 1,3-Benzenedicarboxamide, N'-[[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]]-N,N-dipropyl]- (9CI) (CA INDEX NAME)

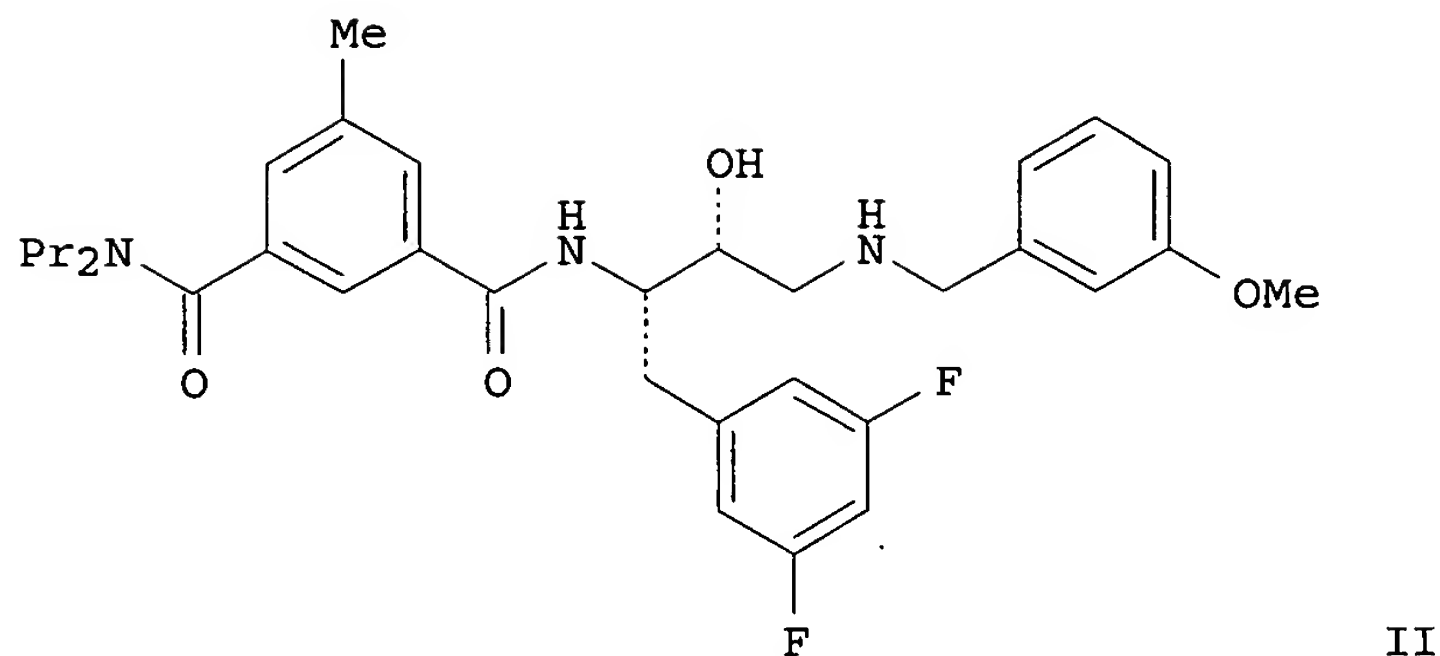
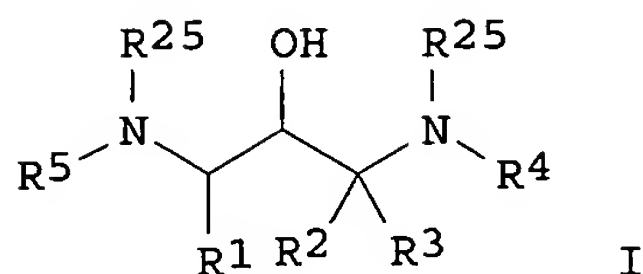
Absolute stereochemistry.



RN 527728-13-8 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO<sub>2</sub>, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO<sub>2</sub>, (un)substituted CH<sub>2</sub>; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC<sub>50</sub> of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 1 of 1-2 series.

IT 158736-49-3,  $\beta$ -Secretase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 158736-49-3 HCAPLUS

CN  $\beta$ -Secretase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 527716-81-0P 527726-39-2P 527728-13-8P  
527728-27-4P 527728-83-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

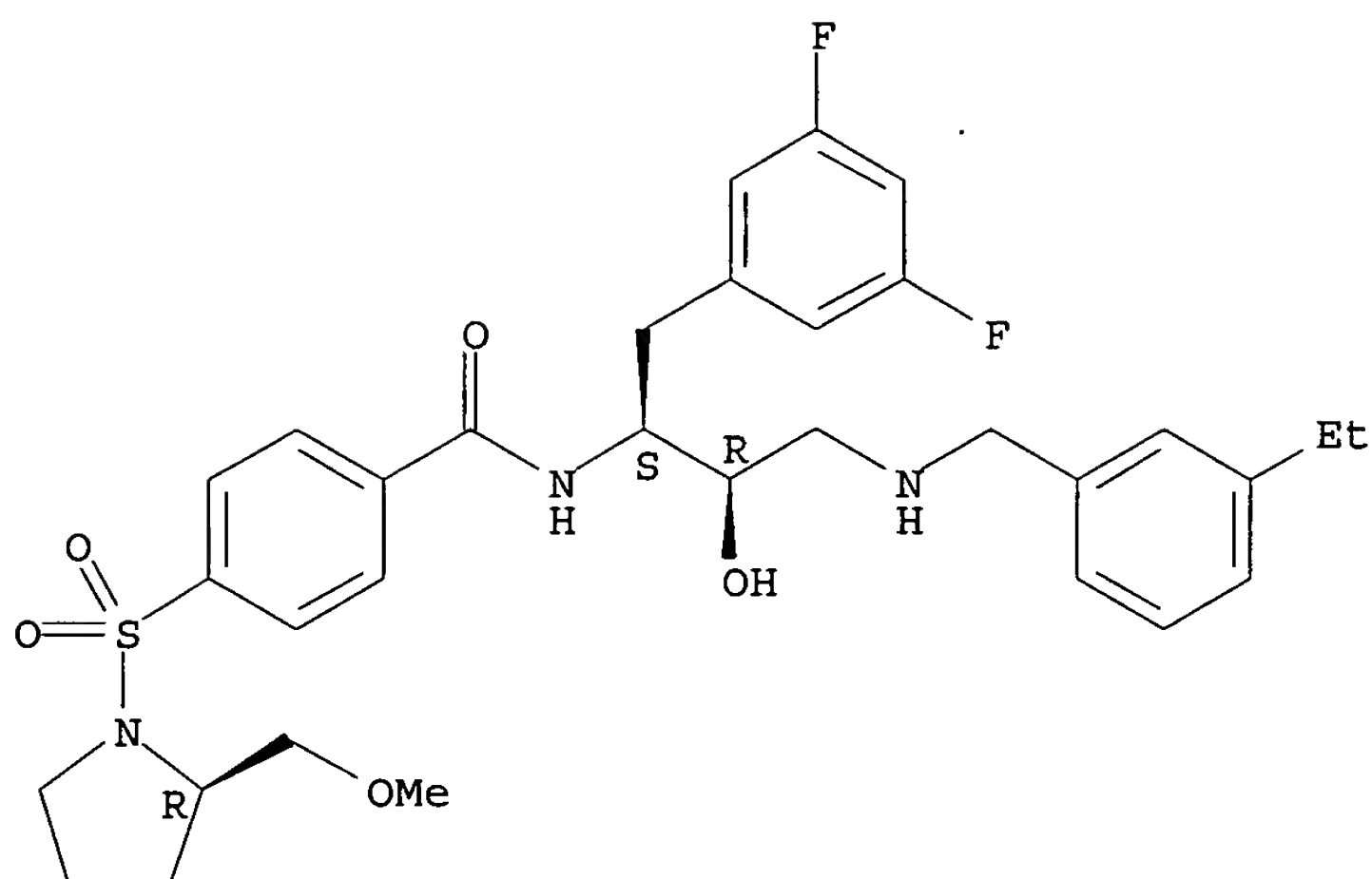
RN 527716-81-0 HCAPLUS

CN 1,3-Benzenedicarboxamide, N'--[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]-N,N-dipropyl]- (9CI) (CA INDEX NAME)

SOURCE: Company  
PCT Int. Appl., 1243 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-US36072	20021108
WO 2003040096	A3	20040506		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004171881	A1	20040902	US 2002-291318	20021108
EP 1453789	A2	20040908	EP 2002-793909	20021108
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
PRIORITY APPLN. INFO.:			US 2001-337122P	P 20011108
			US 2001-344086P	P 20011228
			US 2002-345635P	P 20020103
			WO 2002-US36072	A 20021108

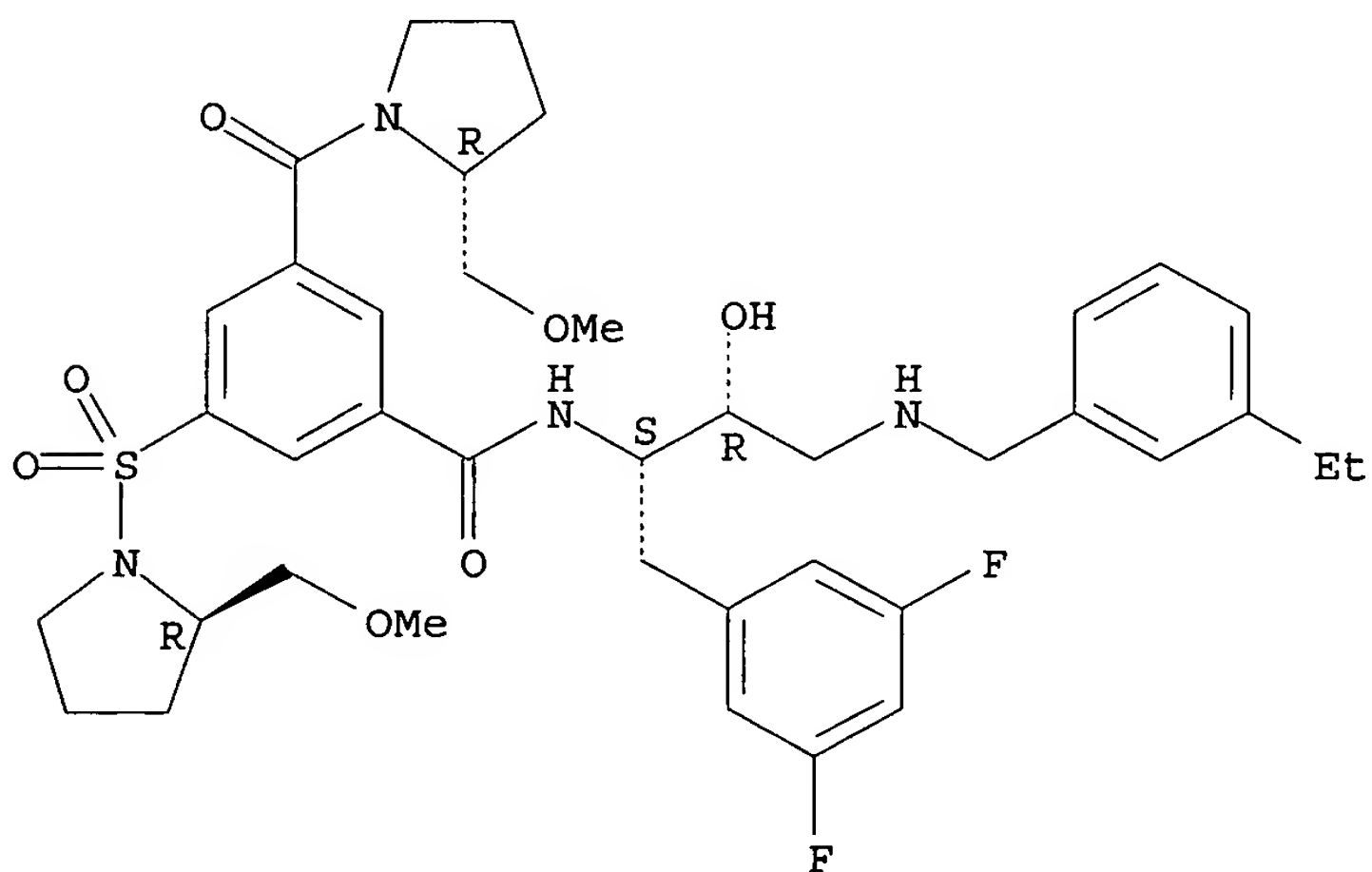
OTHER SOURCE(S): MARPAT 138:385173  
GI



RN 597560-81-1 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-3-[[2R)-2-(methoxymethyl)-1-pyrrolidinyl]carbonyl]-5-[[2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L22 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:376819 HCAPLUS

DOCUMENT NUMBER: 138:385173

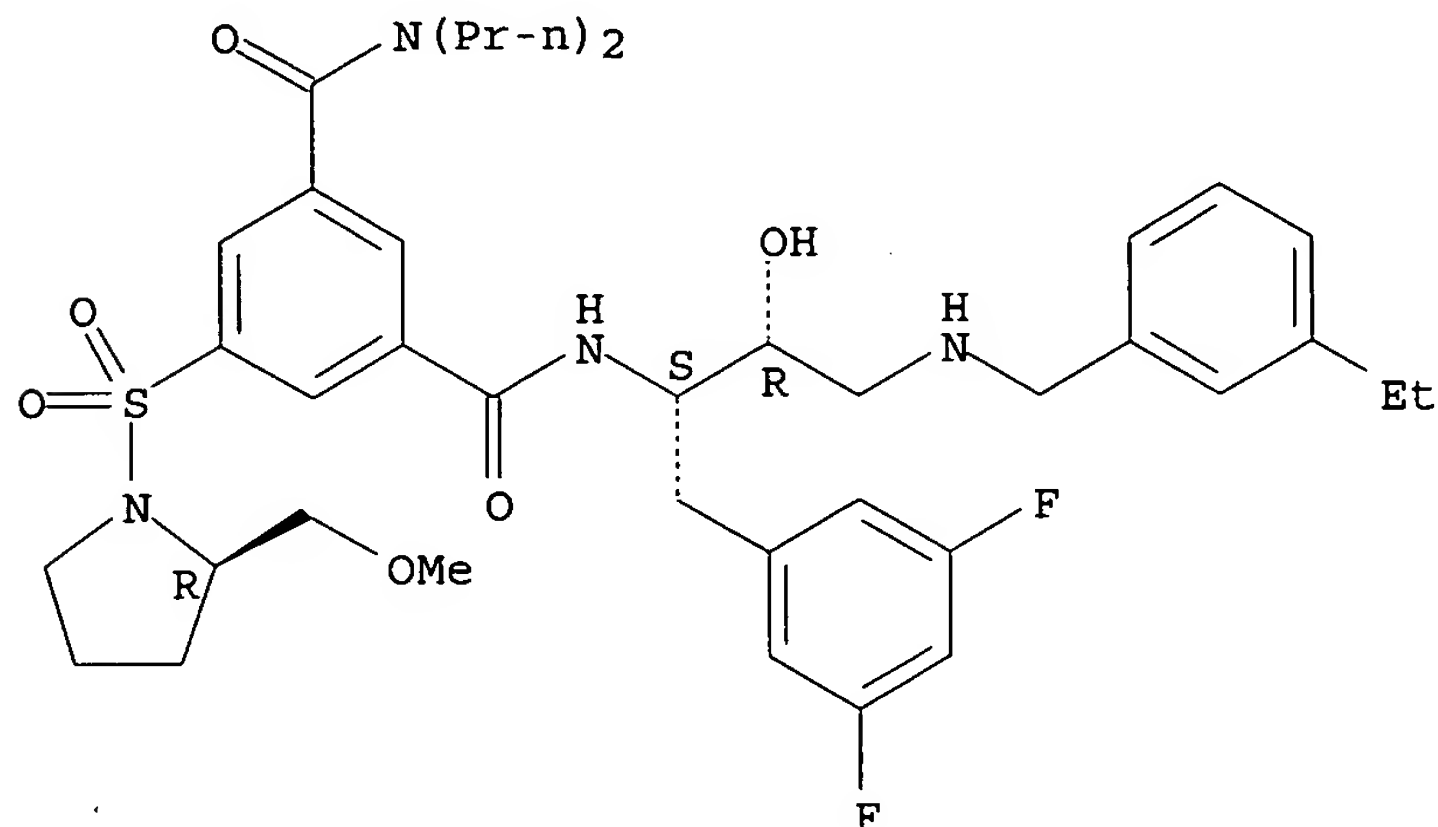
TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease

INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn

CN 1,3-Benzenedicarboxamide, N'-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-5-[[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]-N,N-dipropyl- (9CI) (CA INDEX NAME)

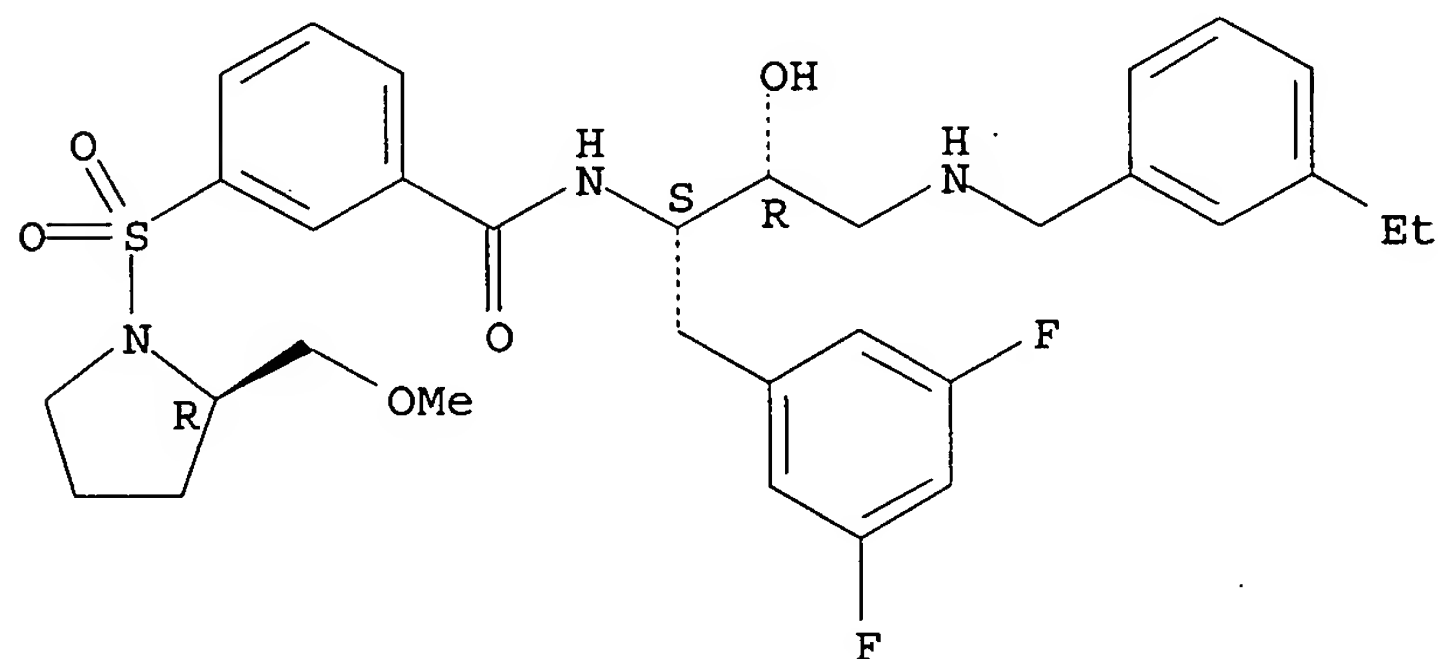
Absolute stereochemistry.



RN 527728-13-8 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-3-[[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 527728-27-4 HCAPLUS

CN Benzamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-4-[[[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

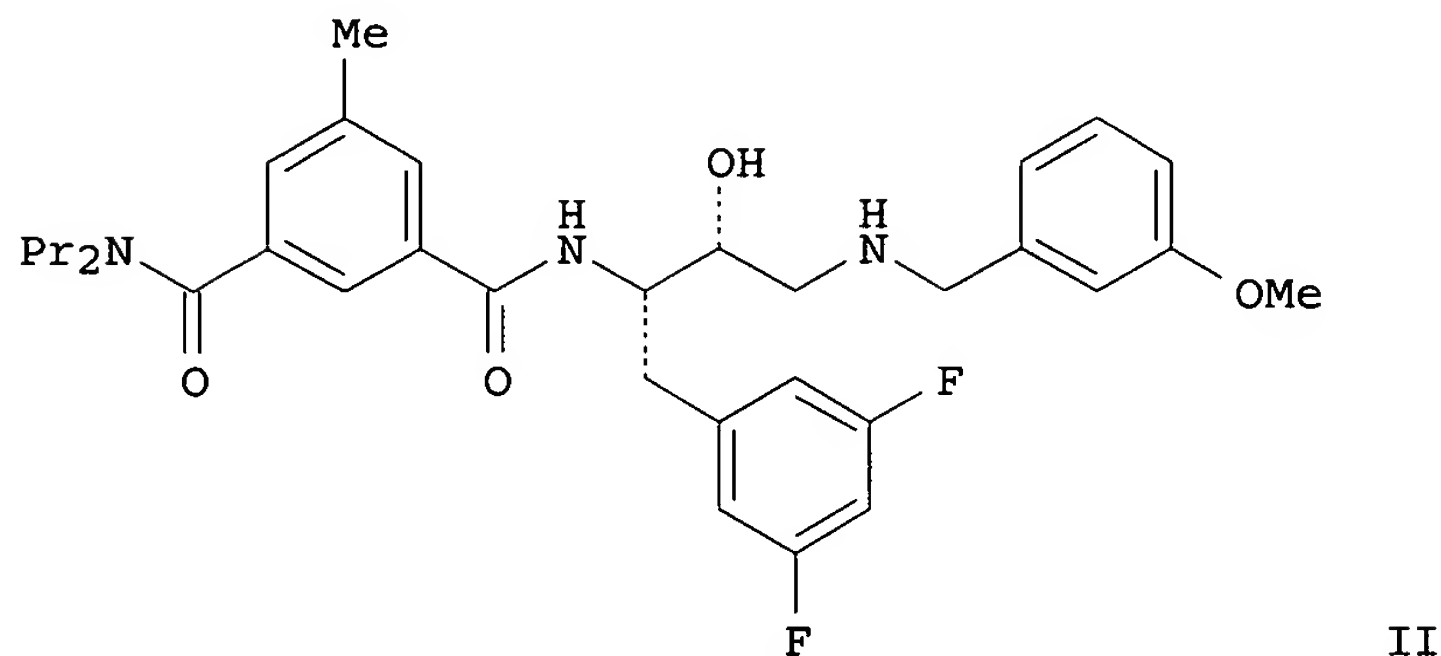
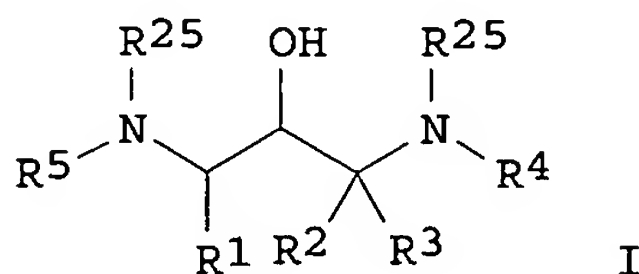
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US 2001-337122P P 20011108  
 US 2001-344086P P 20011228  
 US 2002-345635P P 20020103  
 WO 2002-US36072 A 20021108

## OTHER SOURCE(S):

MARPAT 139:245782

GI



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO2, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO2, (un)substituted CH2; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC50 of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of 1-2 series.

IT 527726-39-2P 527728-13-8P 527728-27-4P  
 597560-81-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

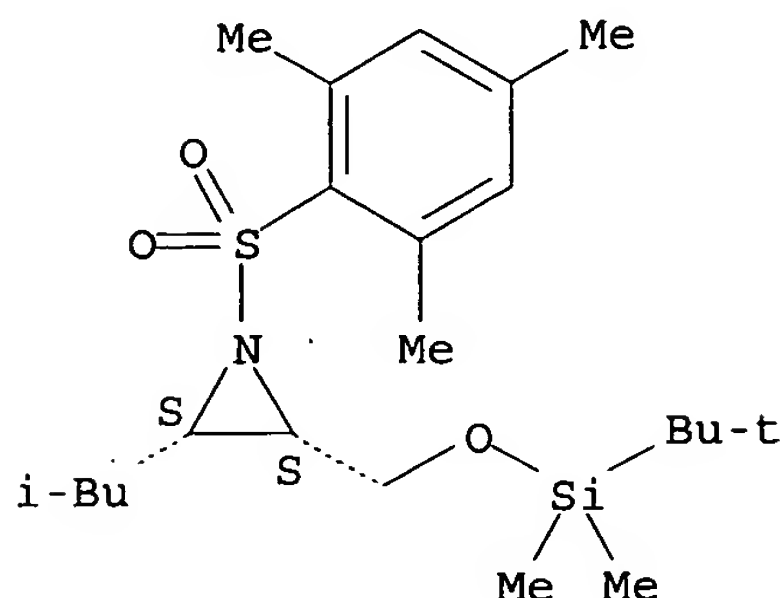
(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 527726-39-2 HCAPLUS



INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:412801 HCAPLUS

DOCUMENT NUMBER: 139:245782

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease

INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 1243 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

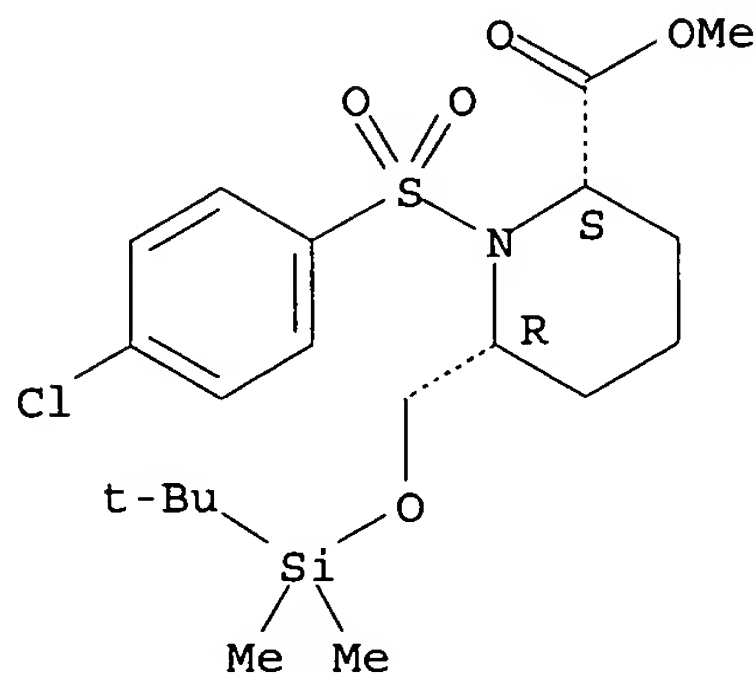
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003040096	A2	20030515	WO 2002-US36072	20021108
WO 2003040096	A3	20040506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

Relative stereochemistry.



L22 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:534852 HCAPLUS

DOCUMENT NUMBER: 140:77384

TITLE: Synthesis of potent  $\beta$ - **secretase** inhibitors containing a hydroxyethylamine dipeptide isostere and their structure-activity relationship studies

AUTHOR(S): Tamamura, Hirokazu; Kato, Terukazu; Otaka, Akira; Fujii, Nobutaka

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, 606-8501, Japan

SOURCE: Organic & Biomolecular Chemistry (2003), 1(14), 2468-2473

CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:77384

AB Several  $\beta$ - **secretase** inhibitors were designed based on hydroxyethylamine dipeptide isostere (HDI) structures and were synthesized by a methodol. using the aza-Payne rearrangement and O,N-acyl transfer reactions to study their structure-activity relationships. Amongst these pseudopeptides, effective compds. were developed as the first  $\beta$ - **secretase** inhibitors containing the HDI transition state mimic with potent enzyme inhibitory activity ( $IC_{50} < 100$  nM).

IT 158736-49-3,  $\beta$ - **Secretase**

RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of hydroxyethylamine dipeptide isostere-based pseudopeptides as potent  $\beta$ - **secretase** inhibitors and their structure-activity relationship studies)

RN 158736-49-3 HCAPLUS

CN  $\beta$ -Secretase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 433922-91-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of hydroxyethylamine dipeptide isostere-based pseudopeptides using aza-Payne rearrangement reaction of a protected aziridine)

RN 433922-91-9 HCAPLUS

CN Aziridine, 2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-(2-methylpropyl)-1-[(2,4,6-trimethylphenyl)sulfonyl]-, (2S,3S)- (9CI) (CA

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004229902	A1	20041118	US 2004-842783	20040511
WO 2004101562	A2	20041125	WO 2004-US14671	20040511
WO 2004101562	A3	20050210		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-470146P P 20030513  
 OTHER SOURCE(S): MARPAT 141:424116  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to a preparation of bridged N-(arylsulfonyl)piperidine derivs. of formula I [wherein: Ar is (hetero)aryl; X is O, NH, NH, or N-aryl, etc.; Y is (CH<sub>2</sub>)<sub>0-3</sub>-R<sub>7</sub>; Z is (CH<sub>2</sub>)<sub>0-3</sub>; R<sub>1</sub> is 1 to 3 independent substituents selected from H, alkyl, CN, NO<sub>2</sub>, NH<sub>2</sub>, etc.; R<sub>2</sub> is H, (cyclo)alkyl, alkylene-O-alkyl, or (hetero)aryl, etc.; R<sub>3</sub> is 1 to 6 independent substituents H, halogen, (cyclo)alkyl, or OCF<sub>3</sub>, etc.; R<sub>4</sub> and R<sub>7</sub> are independently selected from H, alkyl, or aryl; R<sub>4</sub> and R<sub>7</sub> together with the ring carbon atoms may form a cycloalkyl ring; R<sub>5</sub> is (cyclo)alkyl, NH<sub>2</sub>, NH-alkyl, (hetero)aryl, or NH-(hetero)aryl, etc.; R<sub>6</sub> is H, (hetero)aryl, (cyclo)alkyl, or -alkylene-heteroaryl, etc. ], useful as  $\gamma$ -secretase inhibitors. The prepared compds. are useful for the treatment of Alzheimer's disease. For instance, N-(arylsulfonyl)piperidine derivative II (IC<sub>50</sub> is within the range of about 0.1 to about 1.0  $\mu$ M) was prepared via Ru-catalyzed intramol. cyclization of bis(alkenyl)piperidine derivative III, hydrogenation of the obtained azabicyclo[3.3.1]nonene derivative IV, O-carboxylation, and amidation by N-(2-hydroxyethyl)piperazine.

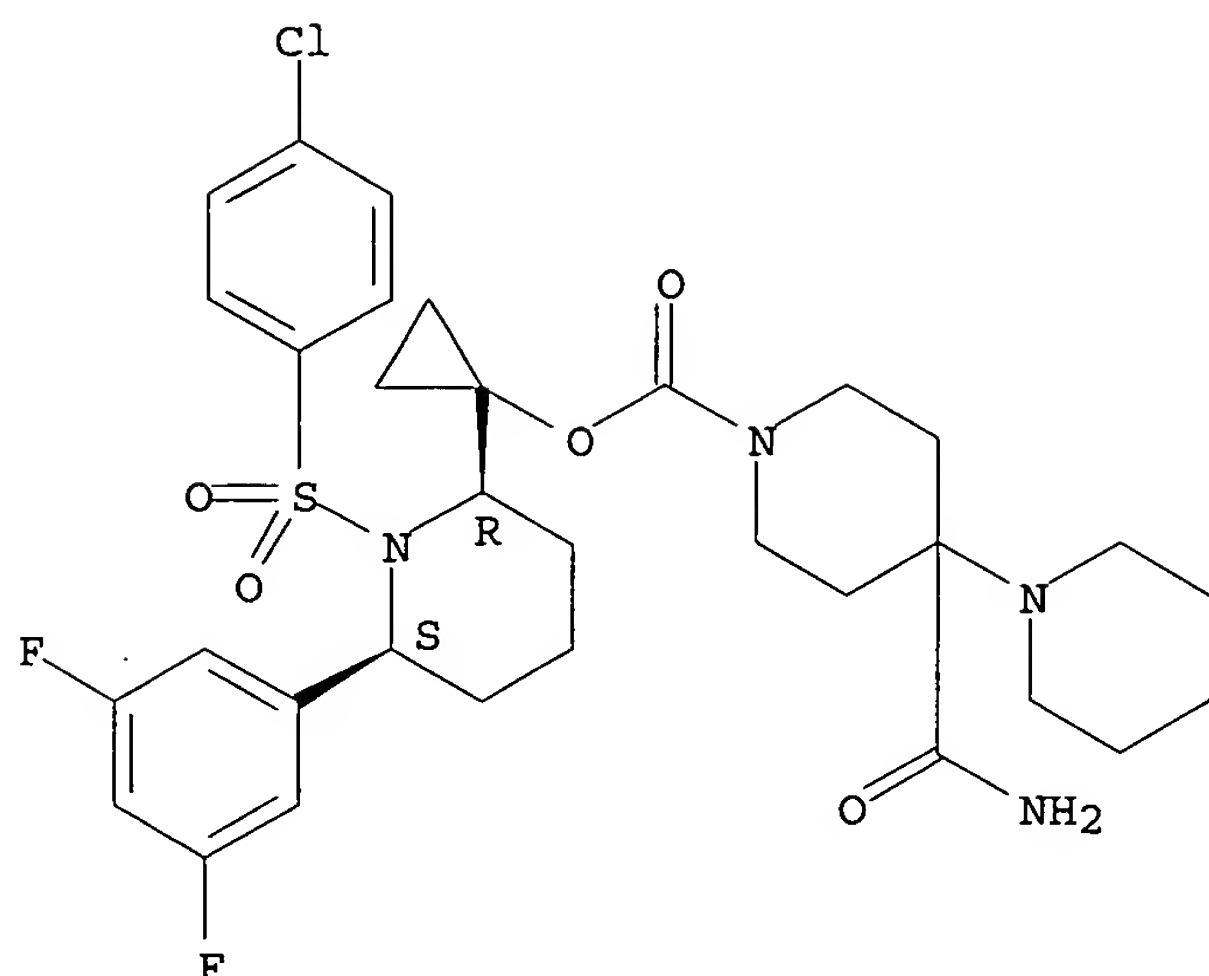
IT 338454-52-7,  $\gamma$ -Secretase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; preparation of bridged N-(arylsulfonyl)piperidine derivs. useful as  $\gamma$ -secretase inhibitors)

RN 338454-52-7 HCAPLUS  
 CN  $\gamma$ -Secretase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 796042-81-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of bridged N-(arylsulfonyl)piperidine derivs. useful as  $\gamma$ -secretase inhibitors)

RN 796042-81-4 HCAPLUS  
 CN 2-Piperidinecarboxylic acid, 1-[(4-chlorophenyl)sulfonyl]-6-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-, methyl ester, (2R,6S)-rel- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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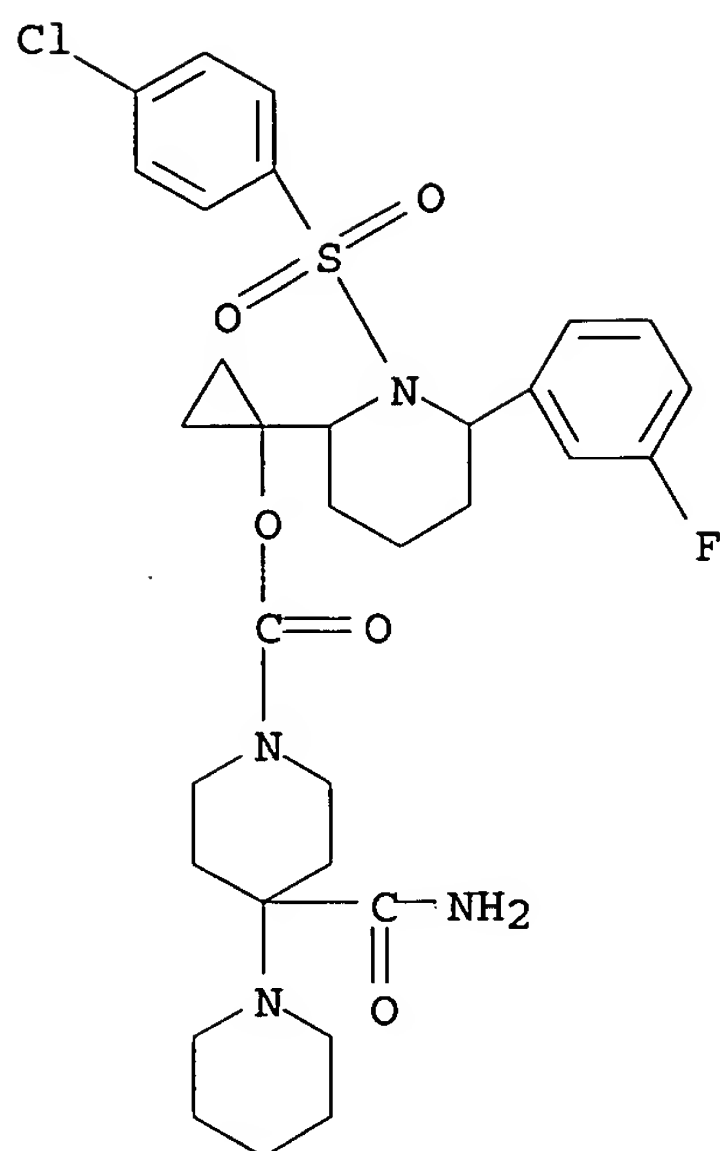
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 L10 STR  
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 L17 25432 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15  
 L18 183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE  
 L19 3443 SEA FILE=HCAPLUS ABB=ON PLU=ON L17  
 L20 2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?  
 L21 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND L20  
 L22 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L16

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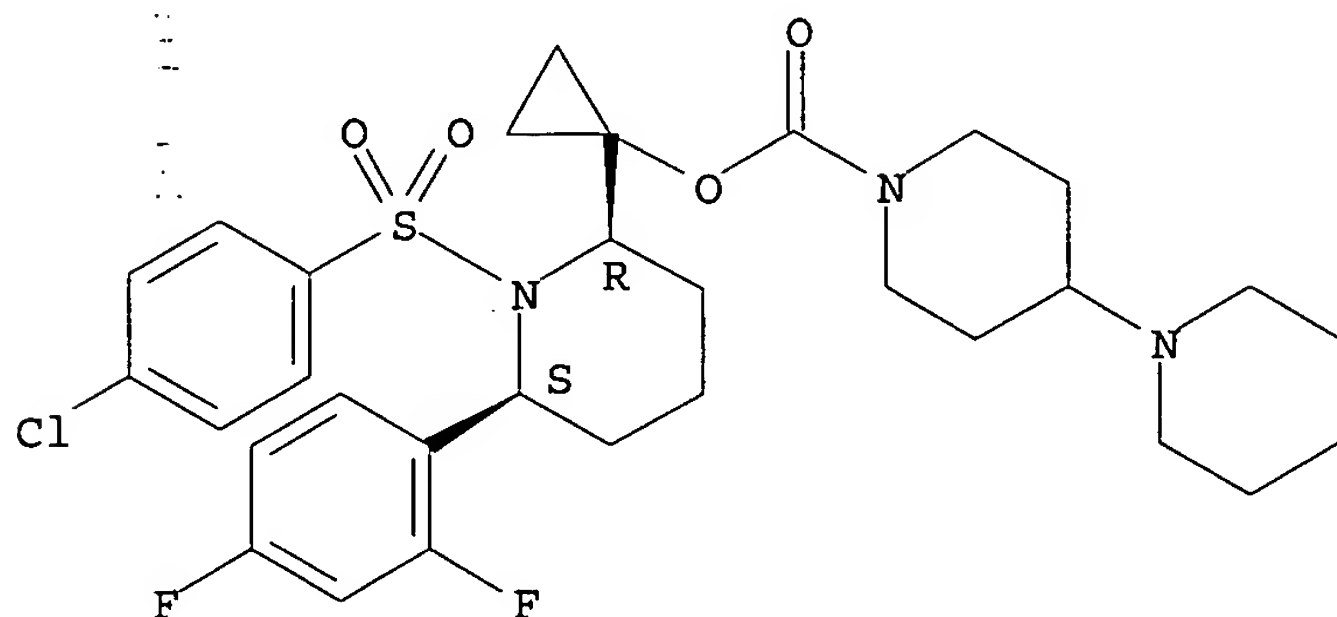
L22 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:999679 HCAPLUS  
 DOCUMENT NUMBER: 141:424116  
 TITLE: A preparation of bridged N-(arylsulfonyl)piperidine derivatives, useful as  $\gamma$ -secretase inhibitors  
 INVENTOR(S): Josien, Hubert B.  
 PATENT ASSIGNEE(S): Schering Corporation, USA  
 SOURCE: U.S. Pat. Appl. Publ., 37 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:



RN 579499-99-3 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(2,4-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

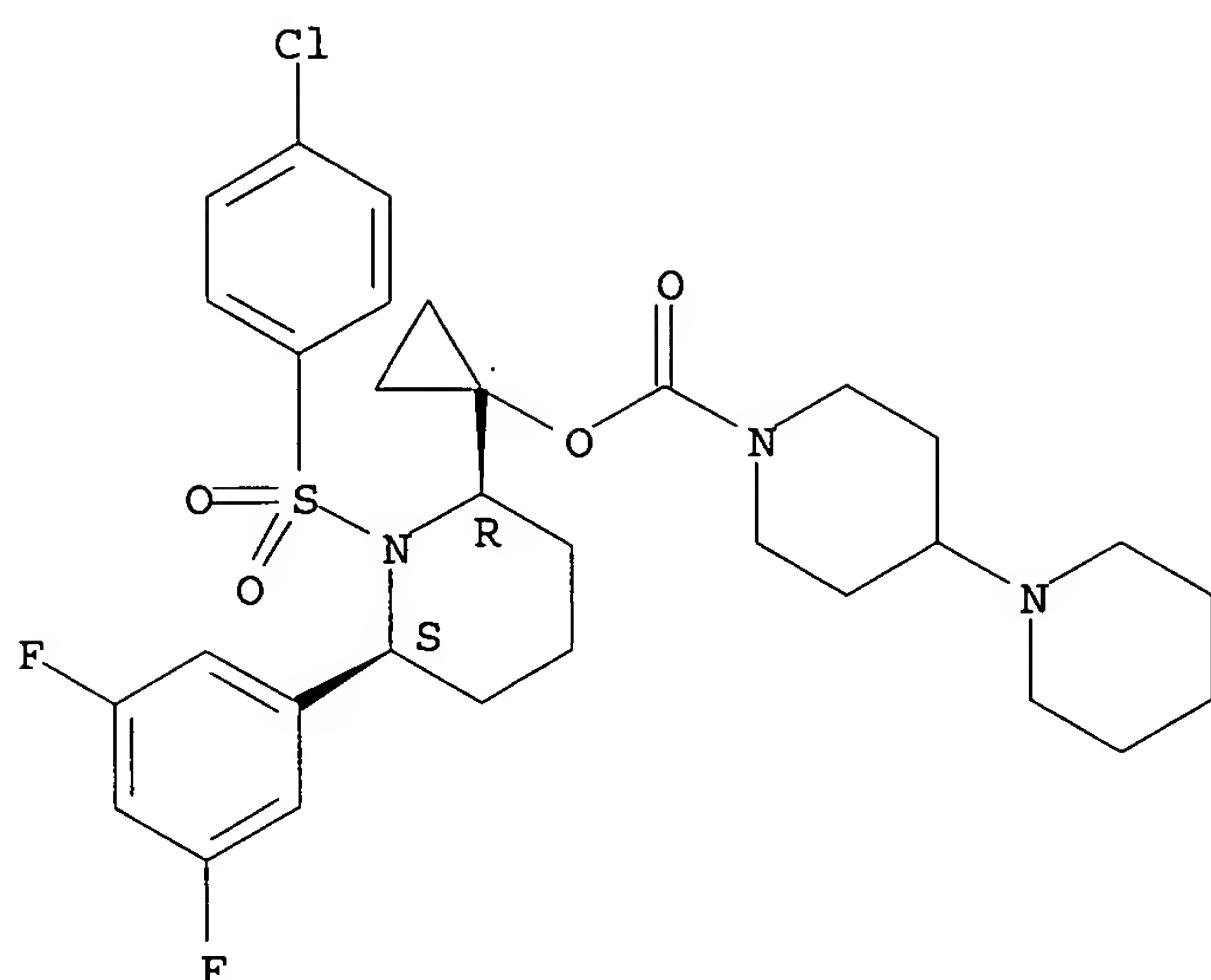
Relative stereochemistry.



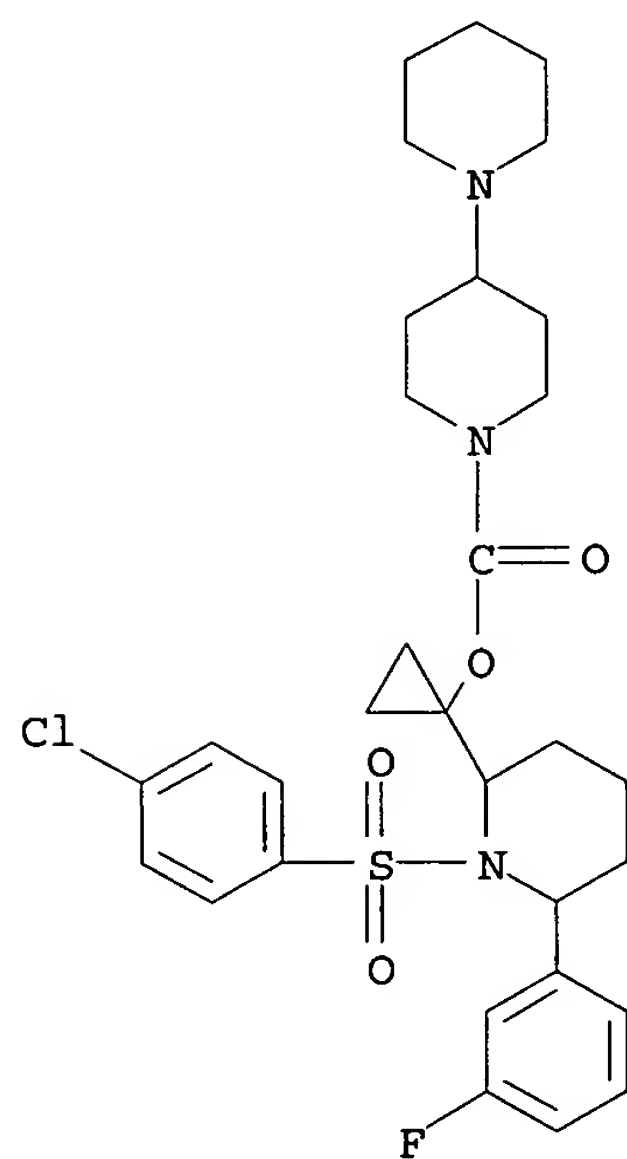
RN 579500-00-8 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

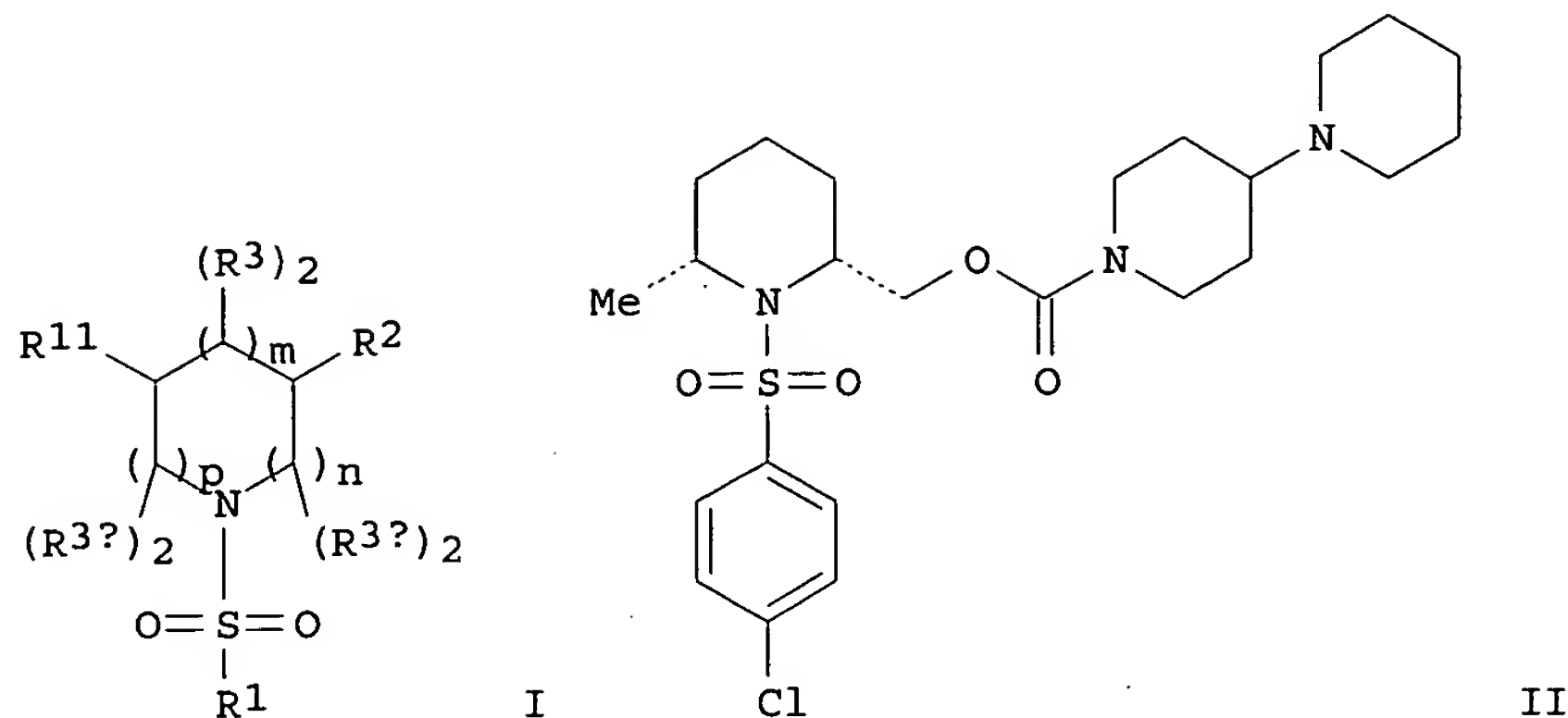


RN 579499-92-6 HCAPLUS  
 CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)



RN 579499-96-0 HCAPLUS  
 CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)

GI



AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un)substitute (hetero)aryl; R3, R3a, and R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as  $\gamma$ -secretase inhibitors, which inhibit the deposition of  $\beta$ -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K<sub>2</sub>CO<sub>3</sub>. The aldehyde was converted to the alc. with NaBH<sub>4</sub> and protected with t-BuPh<sub>2</sub>SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchloroformate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited  $\gamma$ -secretase activity in transfected human APP cells with an IC<sub>50</sub> value in the range of about 0.0002  $\mu$ M to about 15  $\mu$ M. Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

IT 579499-91-5P 579499-92-6P 579499-96-0P  
579499-99-3P 579500-00-8P

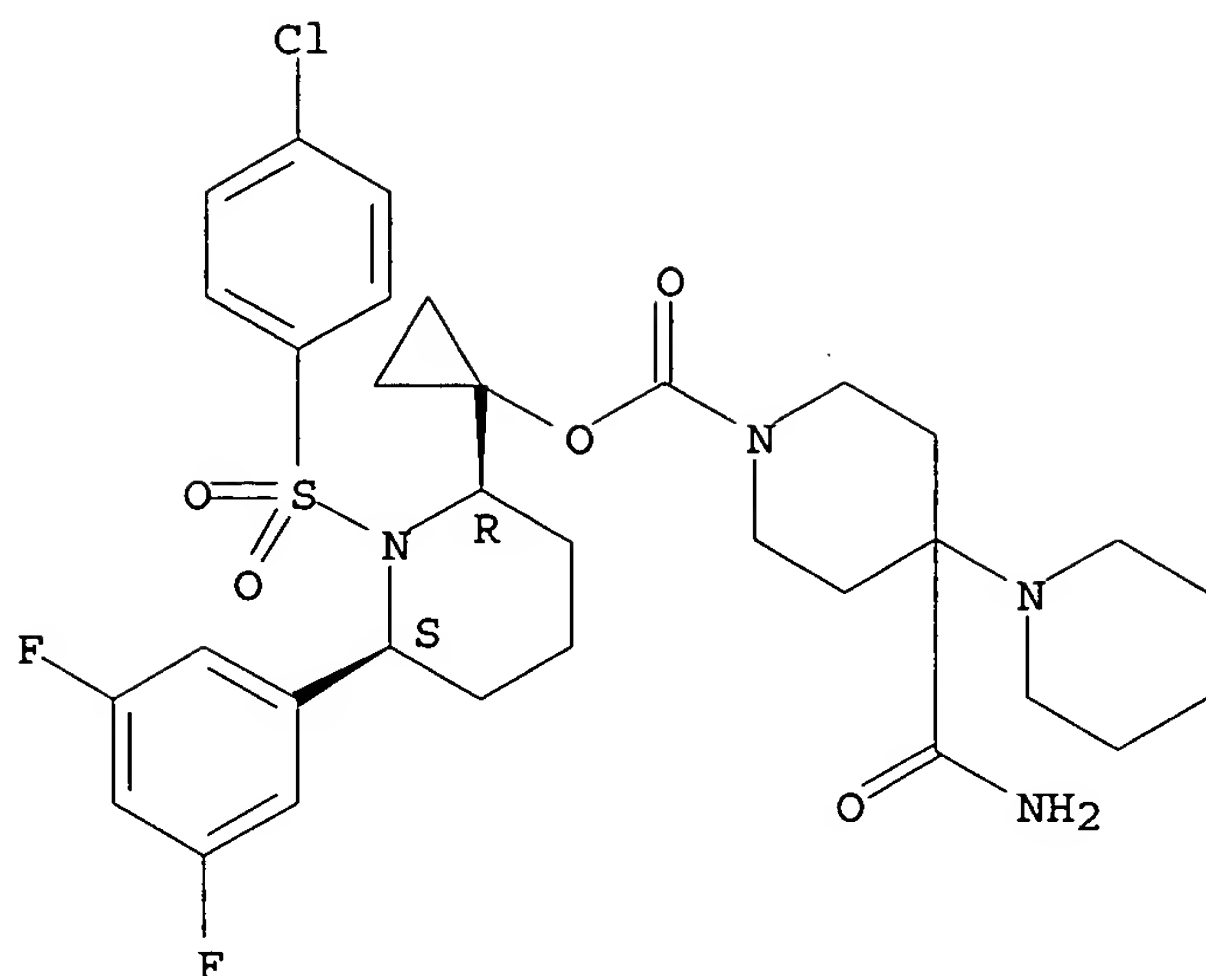
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

( $\gamma$ -secretase inhibitor; preparation of 1-(arylsulfonyl)piperidines as  $\gamma$ -secretase inhibitors for treatment of neurodegenerative diseases)

RN 579499-91-5 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L16 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:633663 HCAPLUS

DOCUMENT NUMBER: 139:179979

TITLE: Preparation of 1-(arylsulfonyl)piperidines as  
γ-secretase inhibitors for treatment of  
neurodegenerative diseasesINVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,  
Elizabeth M.; Clader, John W.; Asberom, Theodros; Guo,  
Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia, Inc.

SOURCE: PCT Int. Appl., 170 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

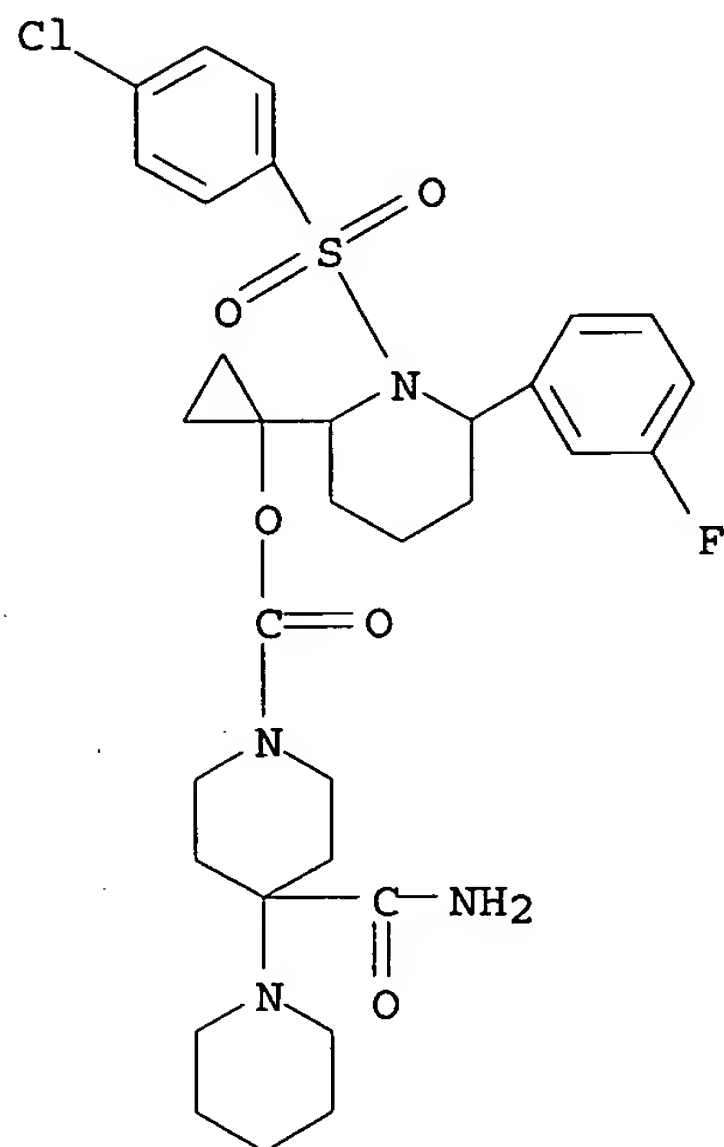
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

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WO 2003066592	A1	20030814	WO 2003-US3471	20030205
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1472223	A1	20041103	EP 2003-737650	20030205
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BR 2003007492	A	20041123	BR 2003-7492	20030205
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			WO 2003-US3471	W 20030205
OTHER SOURCE(S):		MARPAT 139:179979		



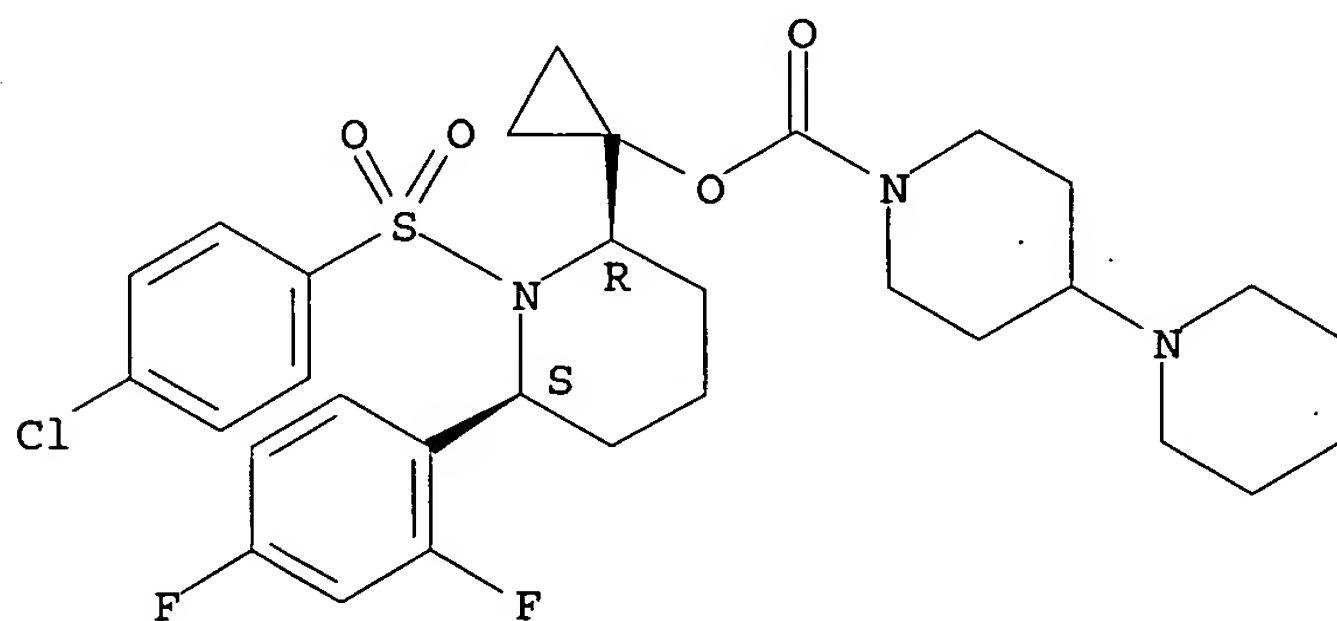
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-,  
1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-  
piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)



RN 579499-99-3 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(2,4-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 579500-00-8 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-,  
1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-  
piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

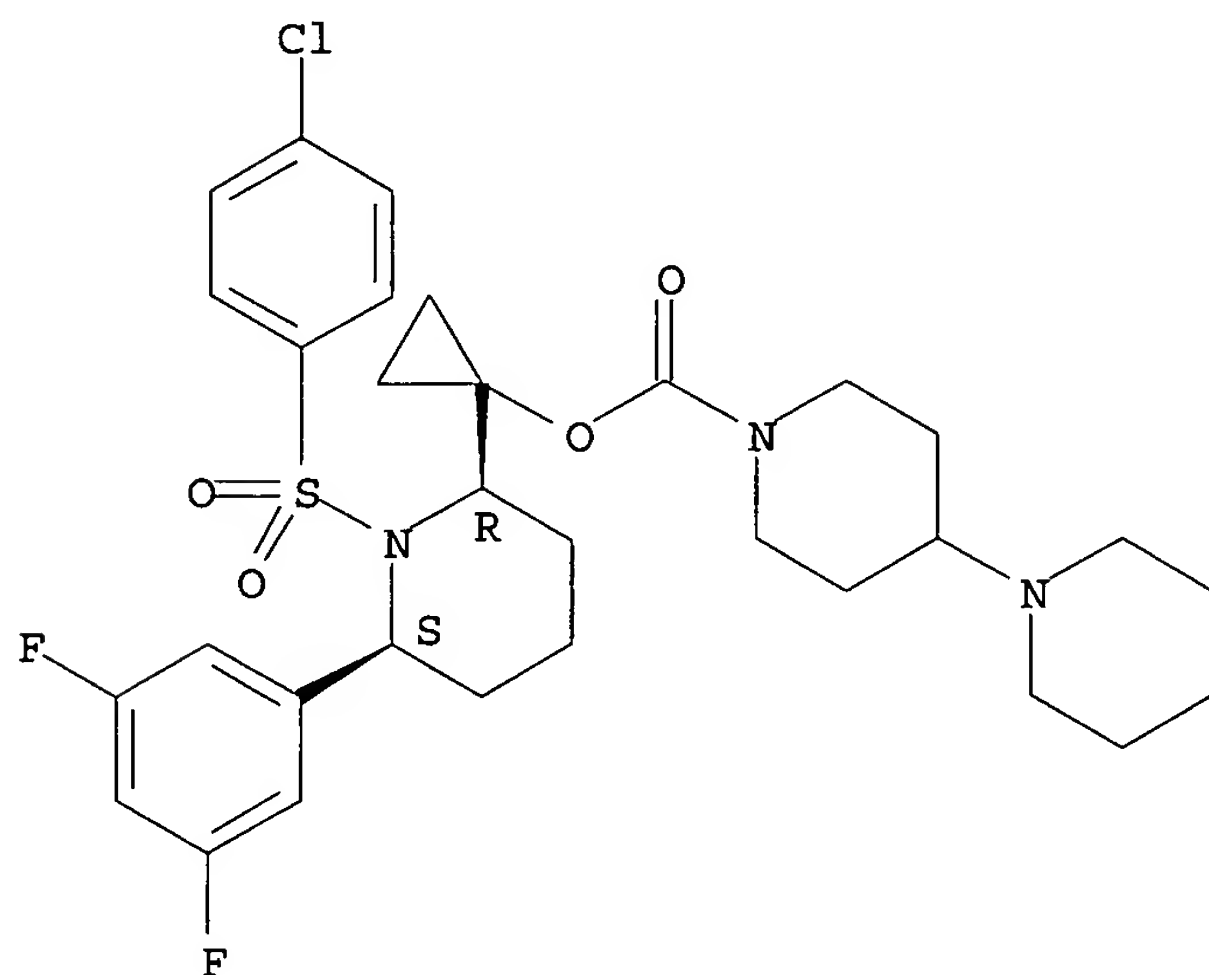
Relative stereochemistry.

$\gamma$ -secretase inhibitors for treatment of neurodegenerative diseases)

RN 579499-91-5 HCAPLUS

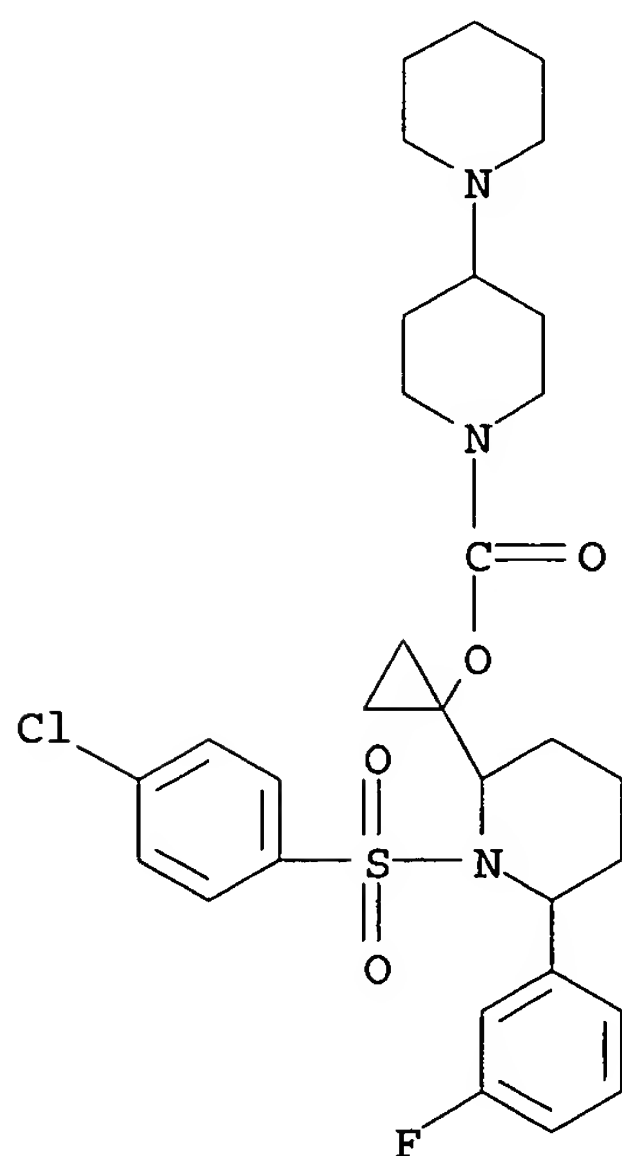
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 579499-92-6 HCAPLUS

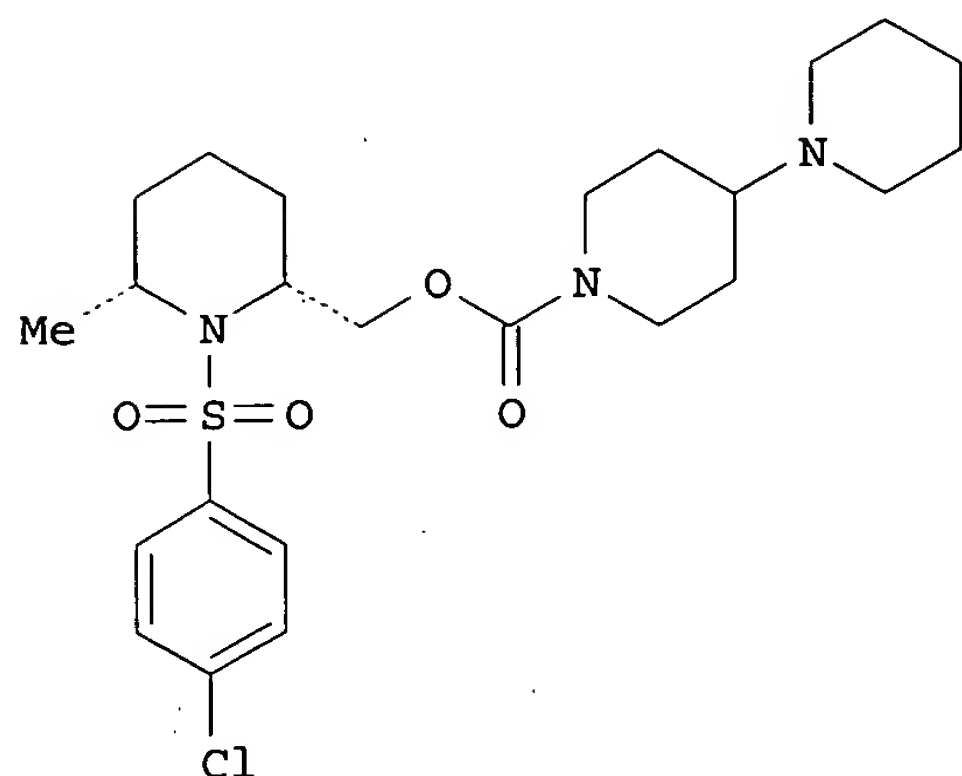
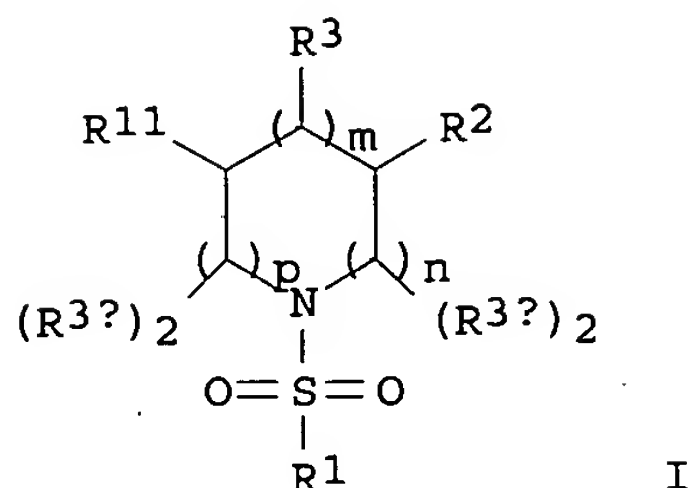
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)



RN 579499-96-0 HCAPLUS

OTHER SOURCE(S):  
GI

MARPAT 141:207066

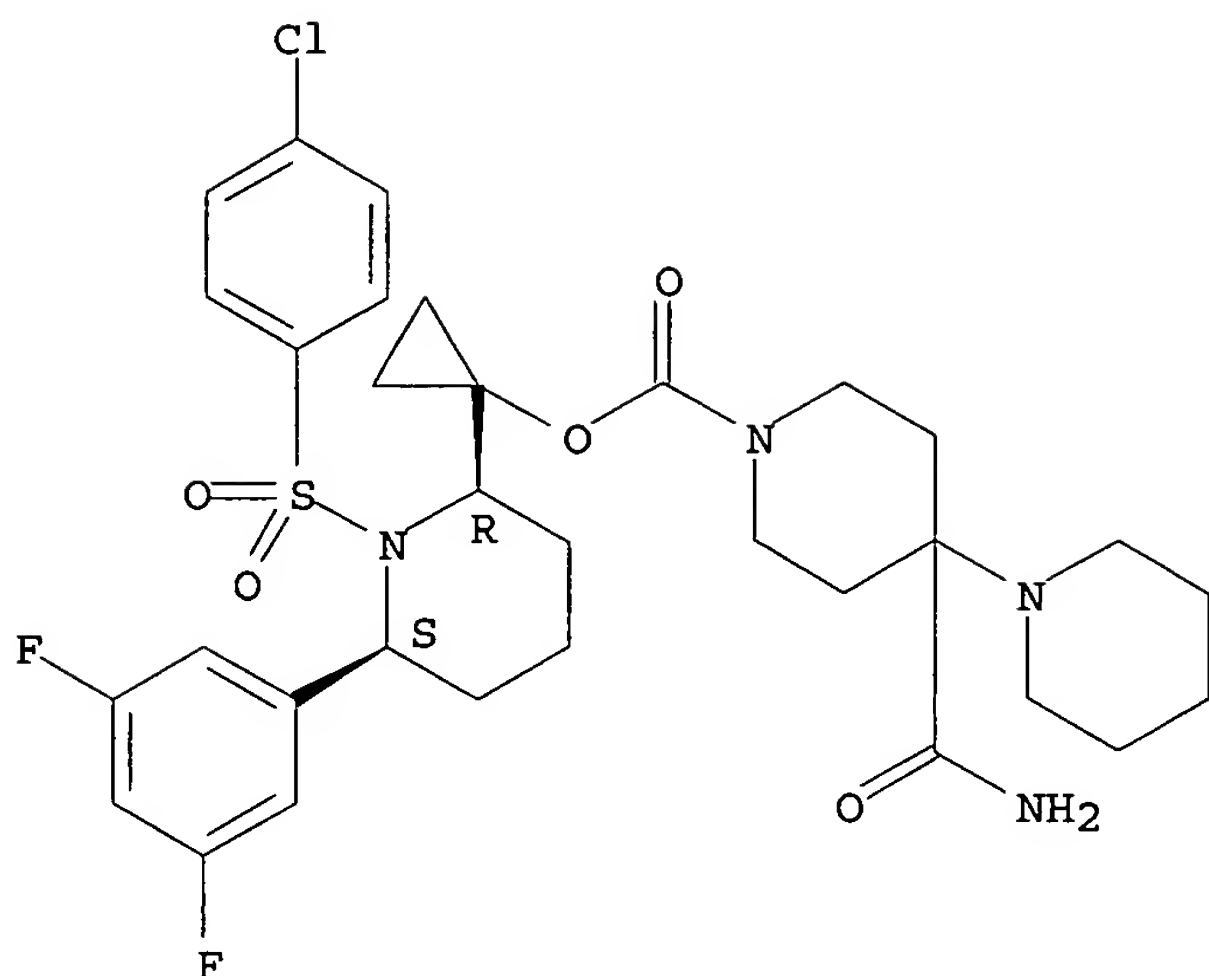


AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un)substituted (hetero)aryl; R3, R3a, and R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as  $\gamma$ -secretase inhibitors, which inhibit the deposition of  $\beta$ -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K<sub>2</sub>CO<sub>3</sub>. The aldehyde was converted to the alc. with NaBH<sub>4</sub> and protected with t-BuPh<sub>2</sub>SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchloroformate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited  $\gamma$ -secretase activity in transfected human APP cells with an IC<sub>50</sub> value in the range of about 0.0002  $\mu$ M to about 15  $\mu$ M. Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

IT 579499-91-5P 579499-92-6P 579499-96-0P  
579499-99-3P 579500-00-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

( $\gamma$ -secretase inhibitor; preparation of (arylsulfonyl)piperidines as



L16 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:722916 HCAPLUS

DOCUMENT NUMBER: 141:207066

TITLE: Preparation of 1-(arylsulfonyl)piperidines as  
γ-secretase inhibitors for treatment of  
neurodegenerative diseasesINVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,  
Elizabeth M.; Clader, John W.; Asberom, Theodros; Guo,  
Tao; Hobbs, Douglas W.PATENT ASSIGNEE(S): Schering-Plough Corporation, USA; Pharmacopeia, Inc.  
SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S.  
Ser. No. 358,898.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

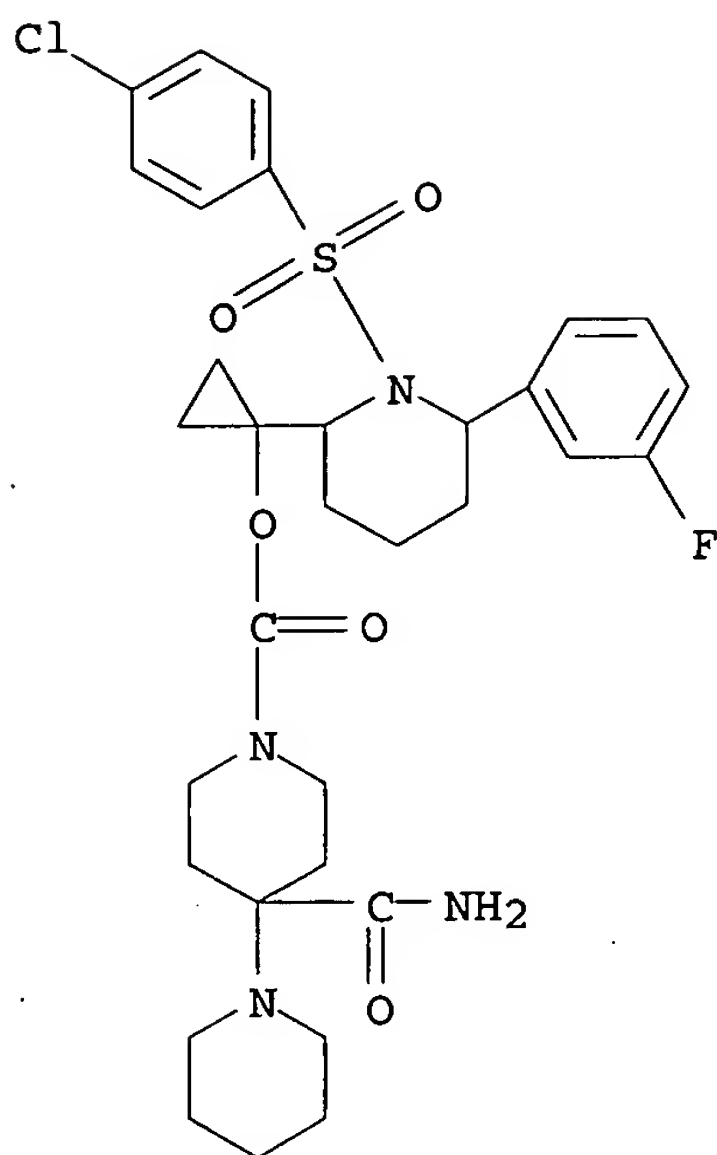
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004171614	A1	20040902	US 2003-663042	20030916
US 2004048848	A1	20040311	US 2003-358898	20030205
WO 2005028440	A1	20050331	WO 2004-US30191	20040915
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PRIORITY APPLN. INFO.: US 2002-355618P P 20020206

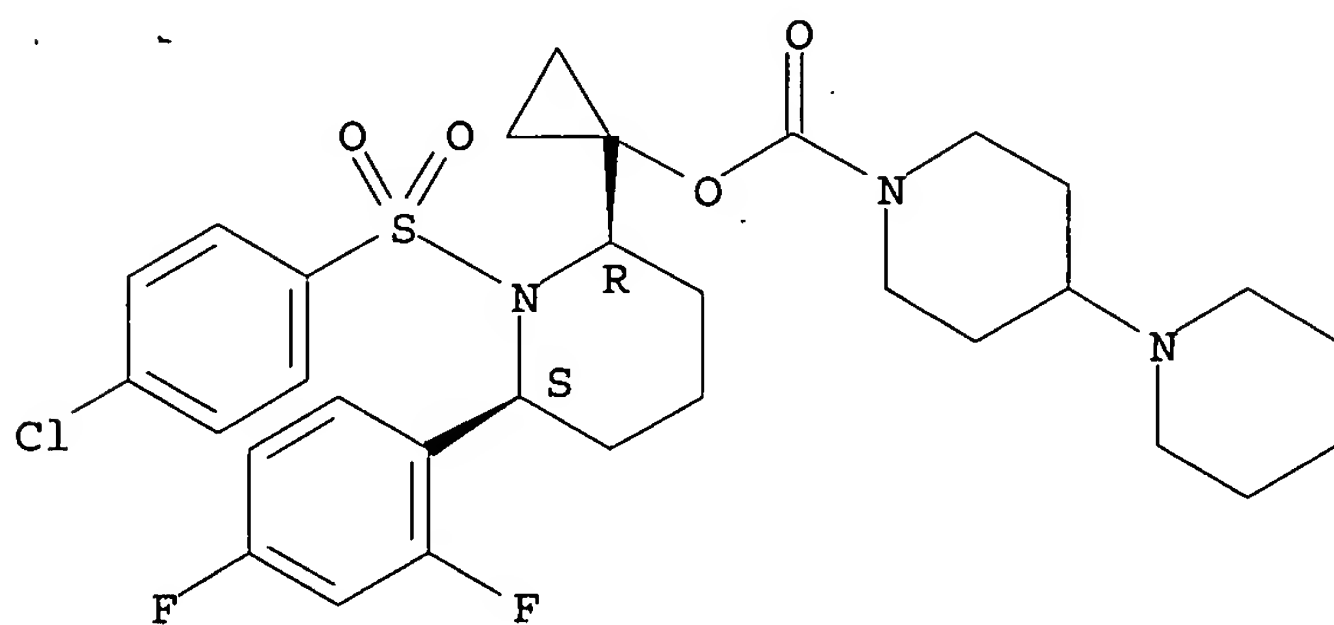
US 2003-358898 A2 20030205



RN 579499-99-3 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(2,4-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



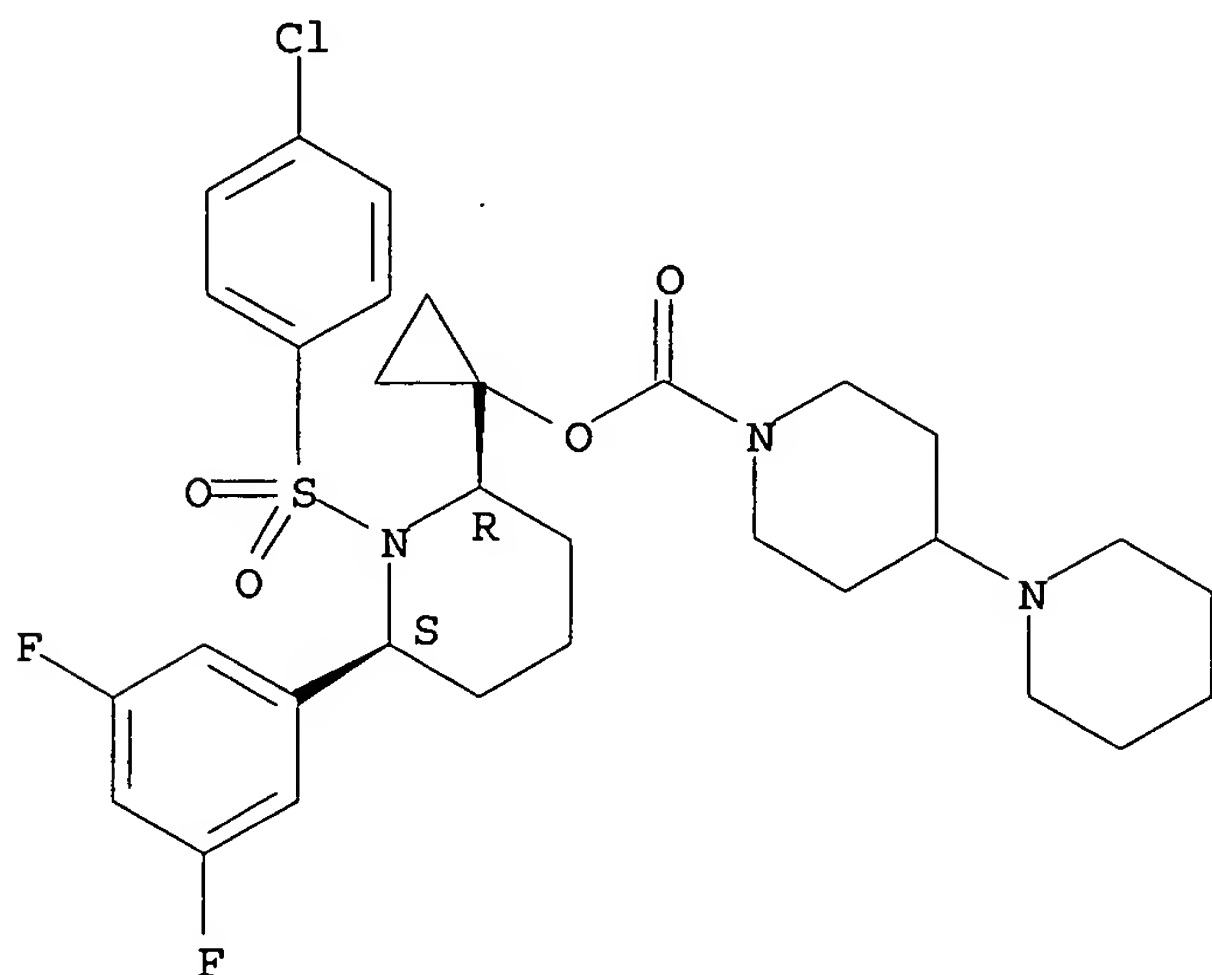
RN 579500-00-8 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-, 1-[(2R,6S)-1-[(4-chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

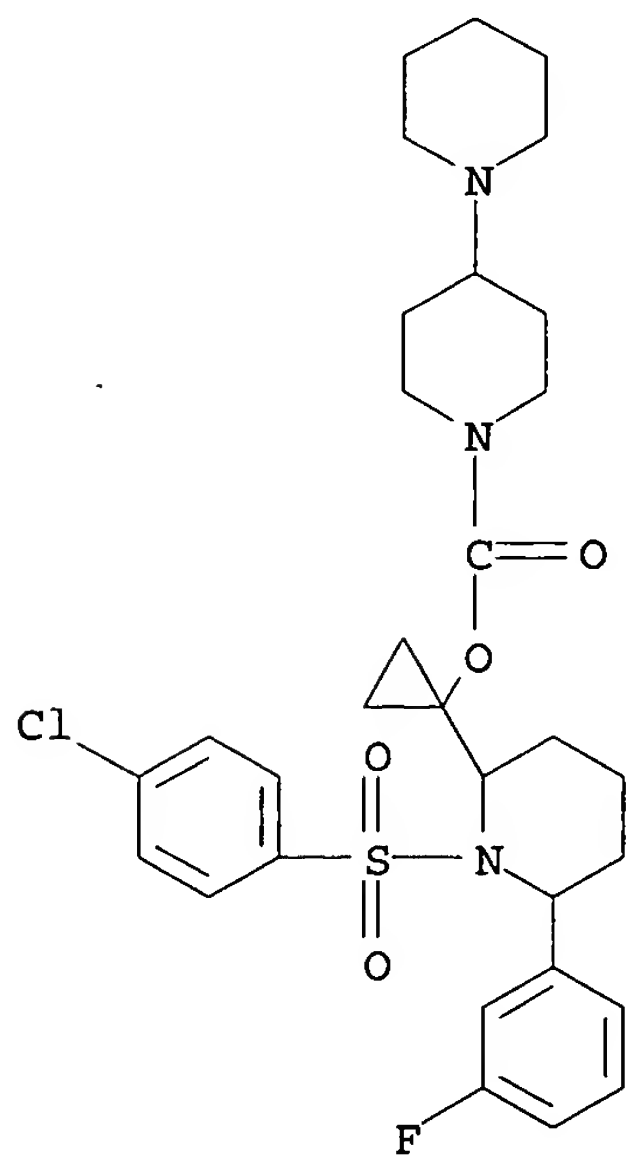
chlorophenyl)sulfonyl]-6-(3,5-difluorophenyl)-2-piperidinyl]cyclopropyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



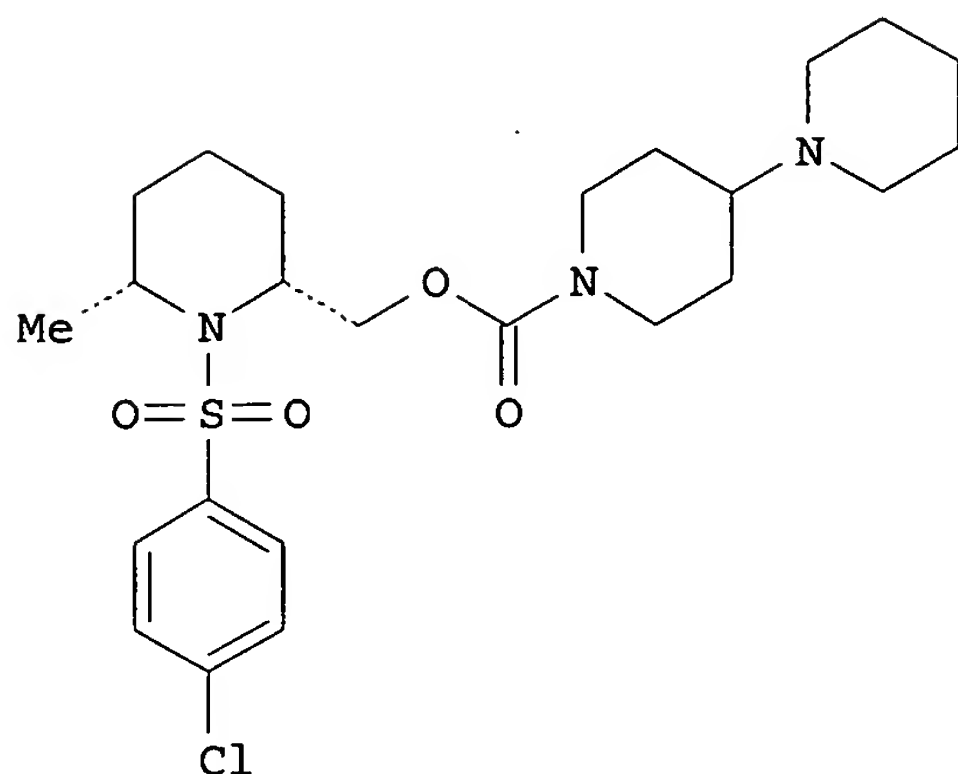
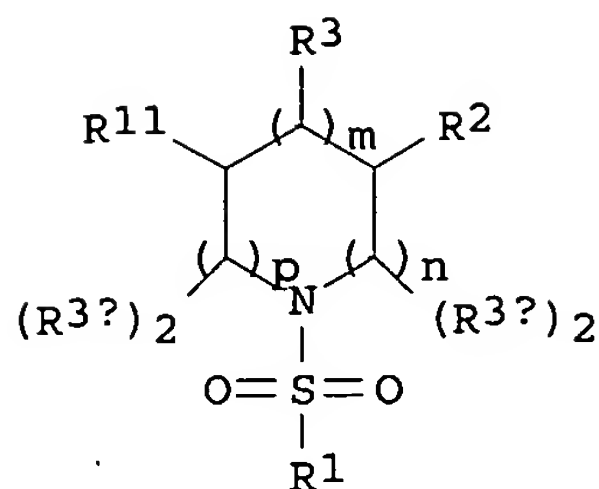
RN 579499-92-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)



RN 579499-96-0 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4'-(aminocarbonyl)-, 1-[1-[(4-chlorophenyl)sulfonyl]-6-(3-fluorophenyl)-2-piperidinyl]cyclopropyl ester (9CI) (CA INDEX NAME)



AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un)substituted (hetero)aryl, etc.; R3 = H, alkyl, OH, alkoxy, etc.; R3a, R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as  $\gamma$ -secretase inhibitors, which inhibit the deposition of  $\beta$ -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K<sub>2</sub>CO<sub>3</sub>. The aldehyde was converted to the alc. with NaBH<sub>4</sub> and protected with t-BuPh<sub>2</sub>SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchlorocarbonate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited  $\gamma$ -secretase activity in transfected human APP cells with an IC<sub>50</sub> value in the range of about 0.0002  $\mu$ M to about 15  $\mu$ M. Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

IT INDEXING IN PROGRESS

IT 579499-91-5P 579499-92-6P 579499-96-0P

579499-99-3P 579500-00-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

( $\gamma$ -secretase inhibitor; preparation of (arylsulfonyl)piperidines as  $\gamma$ -secretase inhibitors for treatment of neurodegenerative diseases)

RN 579499-91-5 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 1-[(2R,6S)-1-[(4-

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

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L16 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15

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L16 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:346733 HCAPLUS

TITLE: Preparation of 1-(arylsulfonyl)piperidines as  
 $\gamma$ -secretase inhibitors for treatment of  
neurodegenerative diseases

INVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,  
Elizabeth M.; Clader, John W.; Asberom, Theodros; Guo,  
Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S): Schering-Plough Corp., USA; Pharmacopeia, Inc.

SOURCE: U.S. Pat. Appl. Publ., 170 pp., Cont.-in-part of U.S.  
Ser. No. 663,042.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

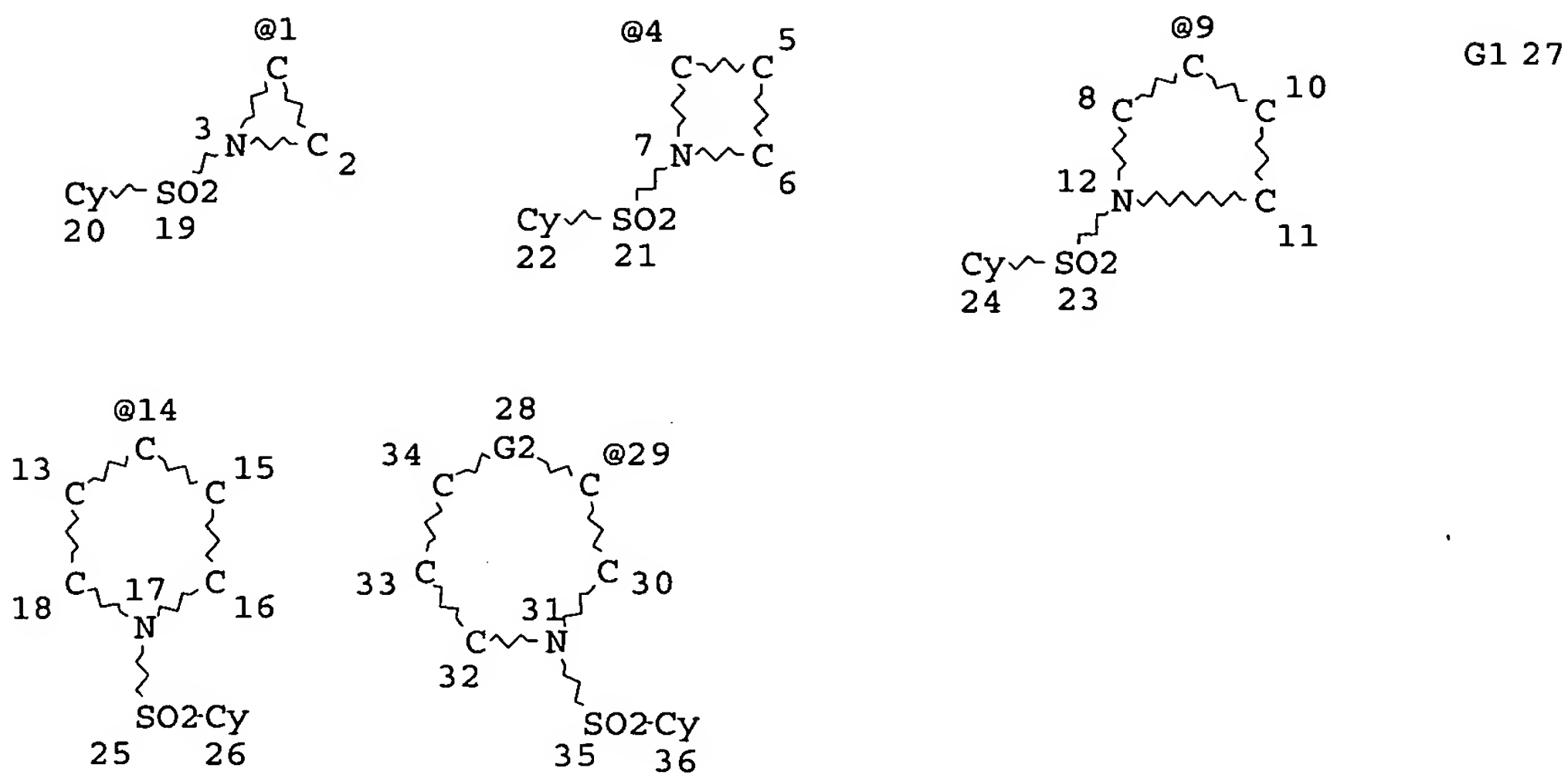
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2005085506	A1	20050421	US 2004-941440	20040915
US 2004048848	A1	20040311	US 2003-358898	20030205
US 2004171614	A1	20040902	US 2003-663042	20030916
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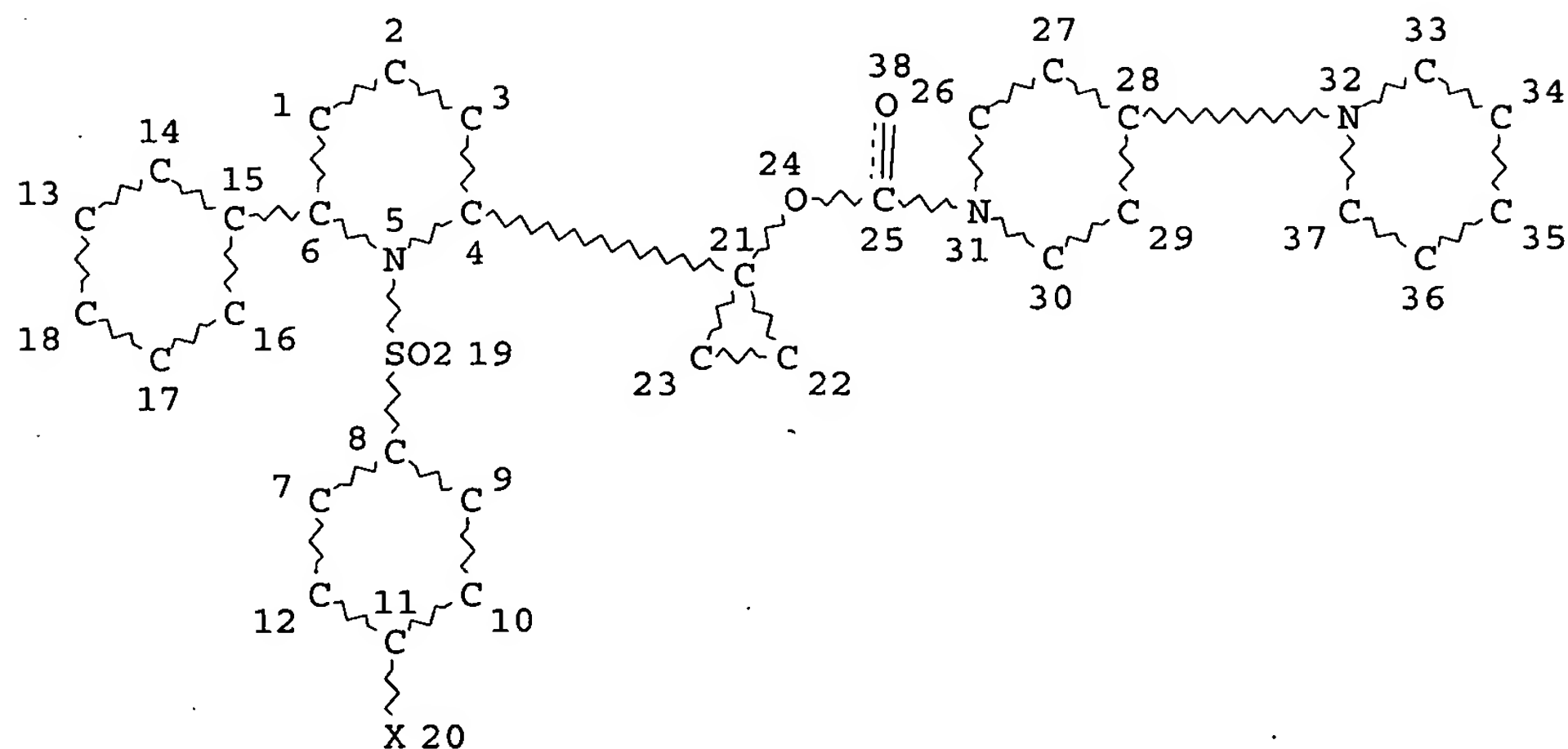




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 NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE  
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NODE ATTRIBUTES:  
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GRAPH ATTRIBUTES:

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FILE 'HCAPLUS' ENTERED AT 15:41:18 ON 13 MAY 2005
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FILE COVERS 1907 - 13 May 2005 VOL 142 ISS 21
FILE LAST UPDATED: 12 May 2005 (20050512/ED)
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L4 STR
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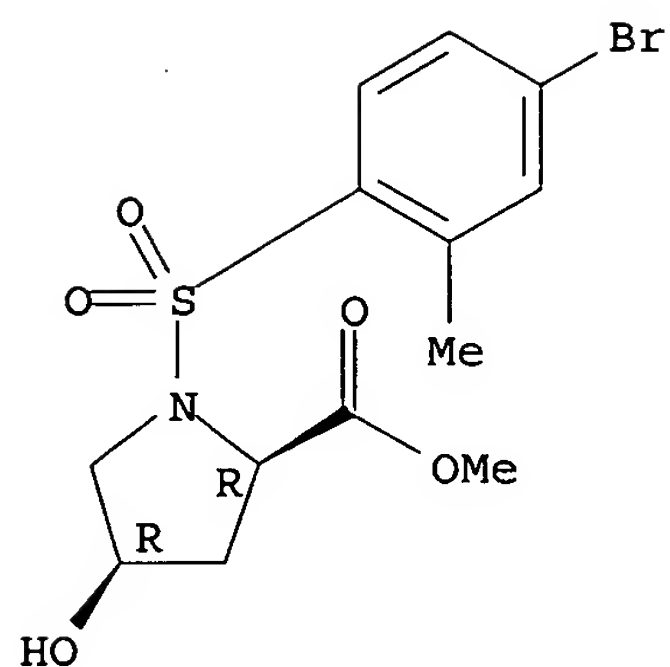
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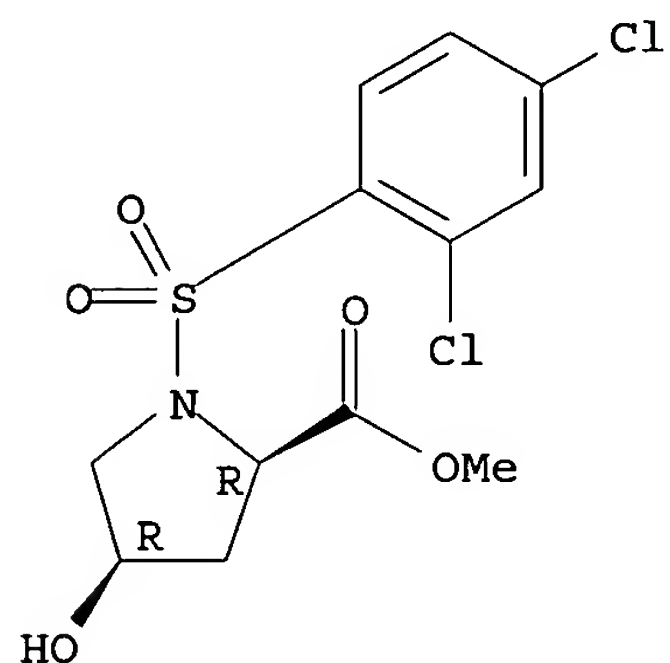
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L10 STR
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RN 204072-52-6 HCAPLUS

CN D-Proline, 1-[(2,4-dichlorophenyl)sulfonyl]-4-hydroxy-, methyl ester,  
(4R)- (9CI) (CA INDEX NAME)

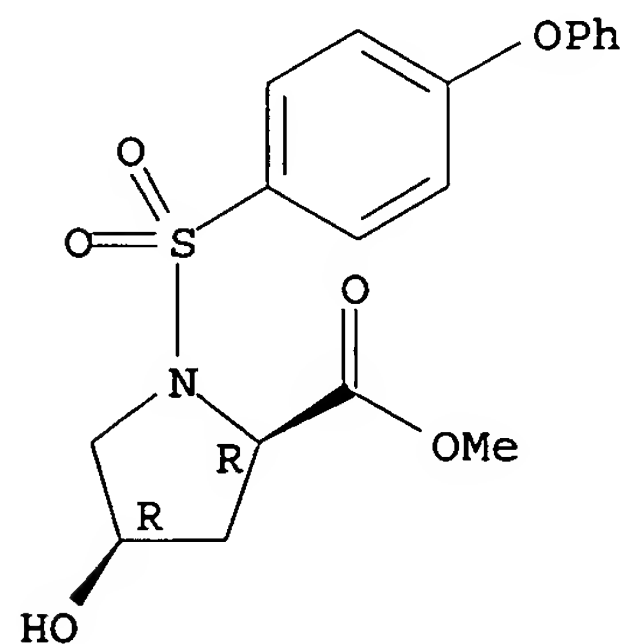
Absolute stereochemistry.



RN 204072-55-9 HCAPLUS

CN D-Proline, 4-hydroxy-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4R)-  
(9CI) (CA INDEX NAME)

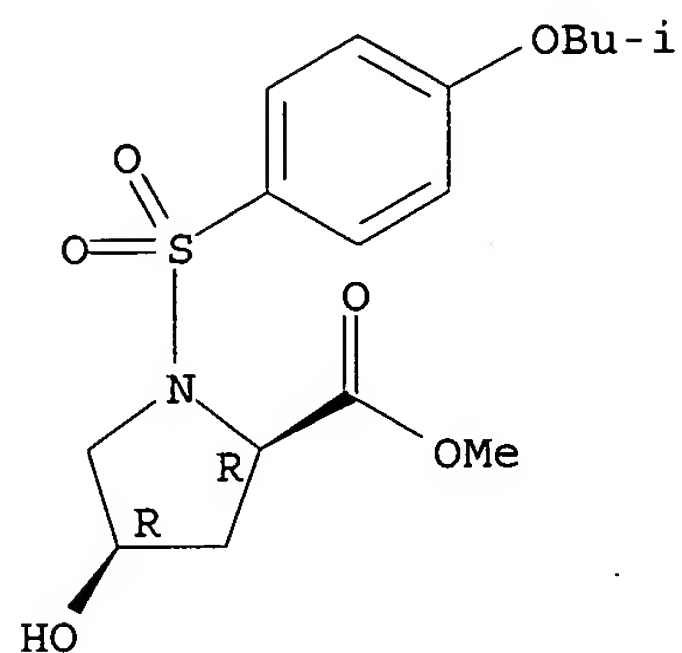
Absolute stereochemistry.



RN 204072-56-0 HCAPLUS

CN D-Proline, 4-hydroxy-1-[[4-(2-methylpropoxy)phenyl]sulfonyl]-, methyl  
ester, (4R)- (9CI) (CA INDEX NAME)

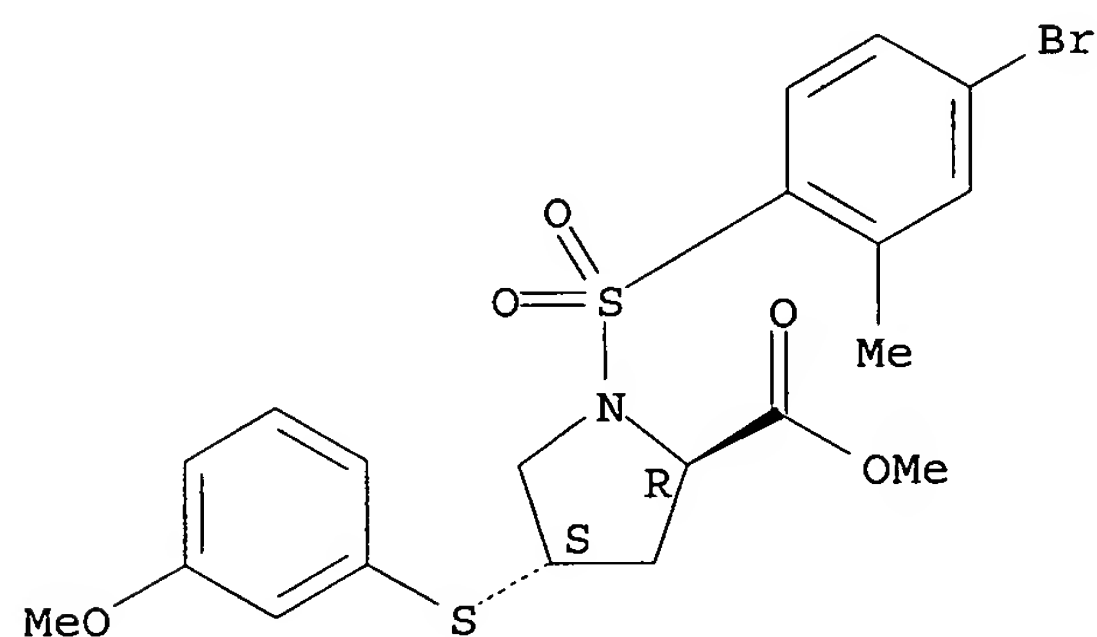
Absolute stereochemistry.



RN 204072-57-1 HCAPLUS

CN D-Proline, 1-[(4-bromo-2-methylphenyl)sulfonyl]-4-[(3-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

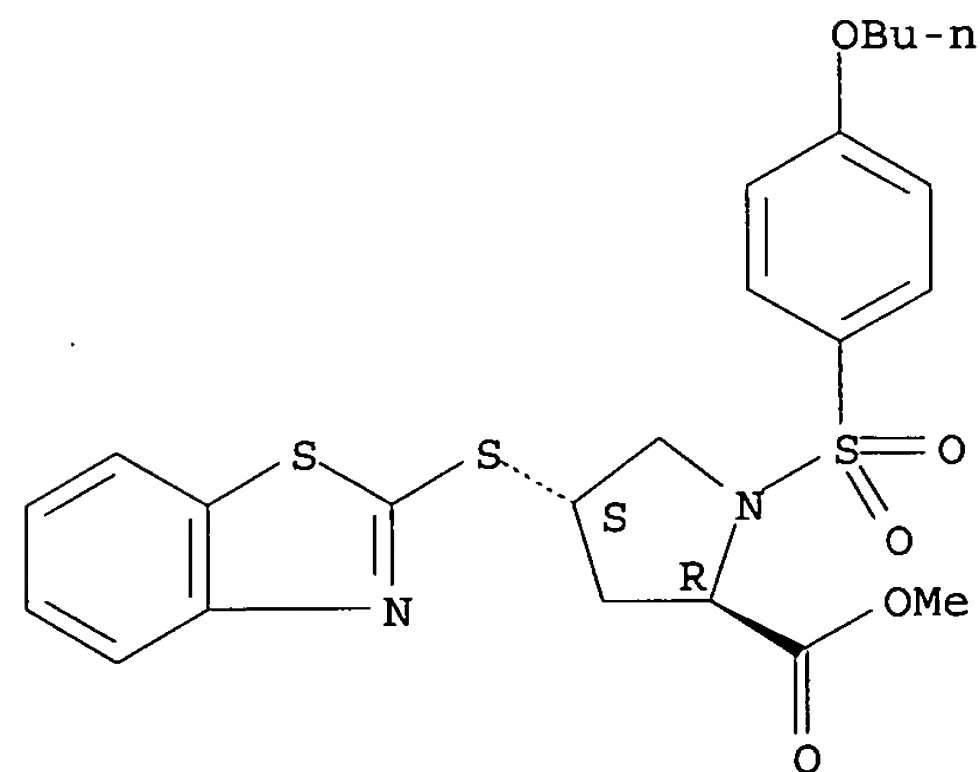
Absolute stereochemistry.



RN 204072-58-2 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

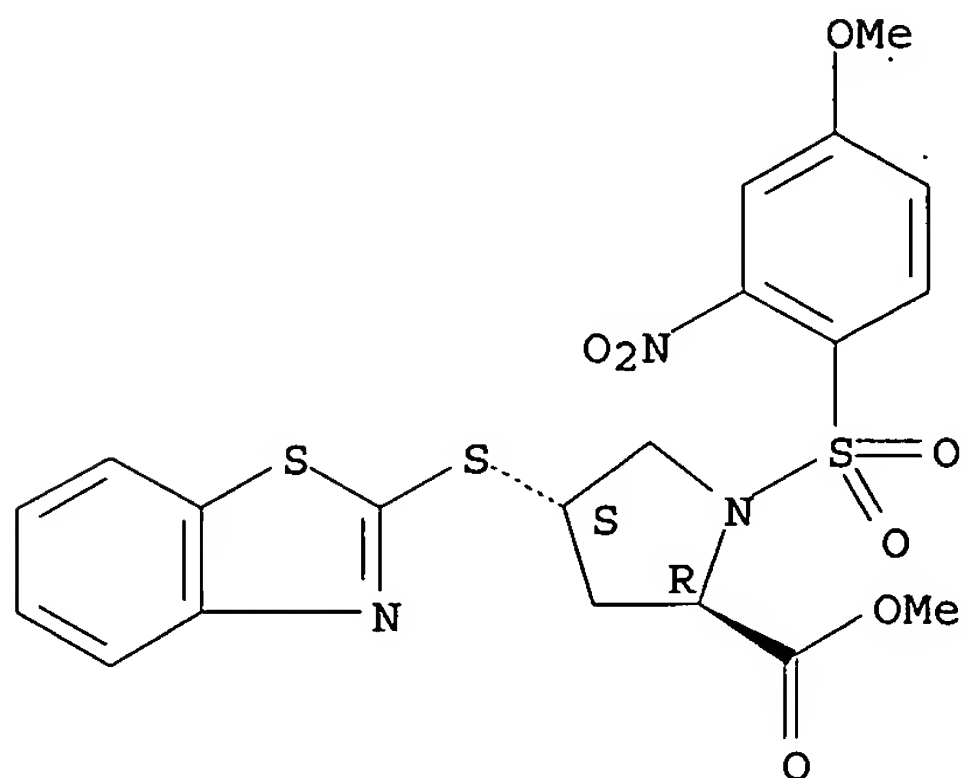
Absolute stereochemistry.



RN 204072-59-3 HCAPLUS

CN D-Proline, 4-(2-benzothiazolylthio)-1-[(4-methoxy-2-nitrophenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

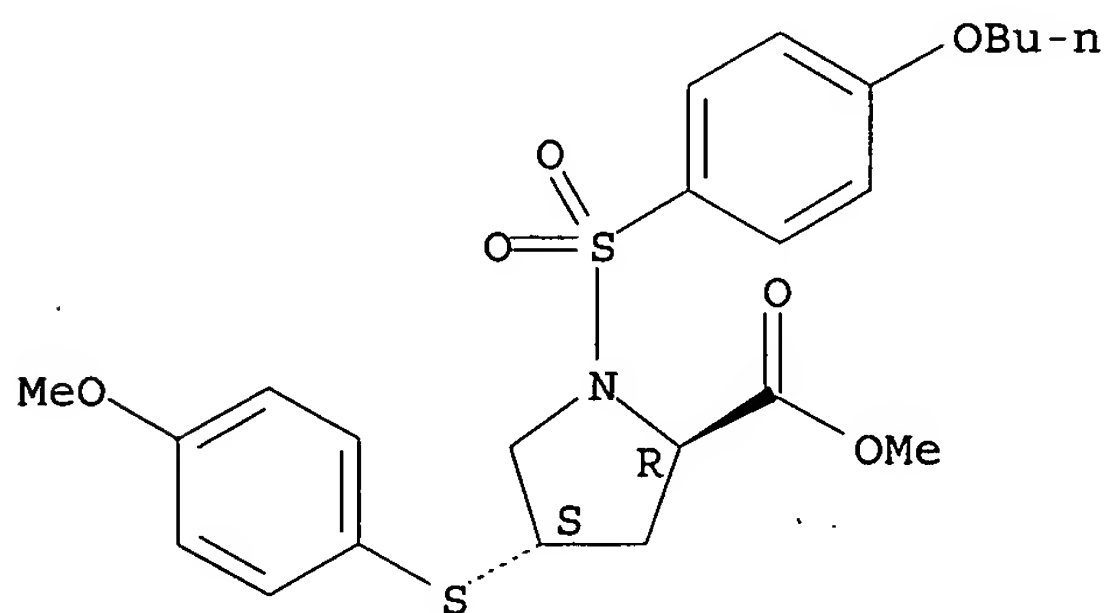
Absolute stereochemistry.



RN 204072-60-6 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(4-methoxyphenyl)thio]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

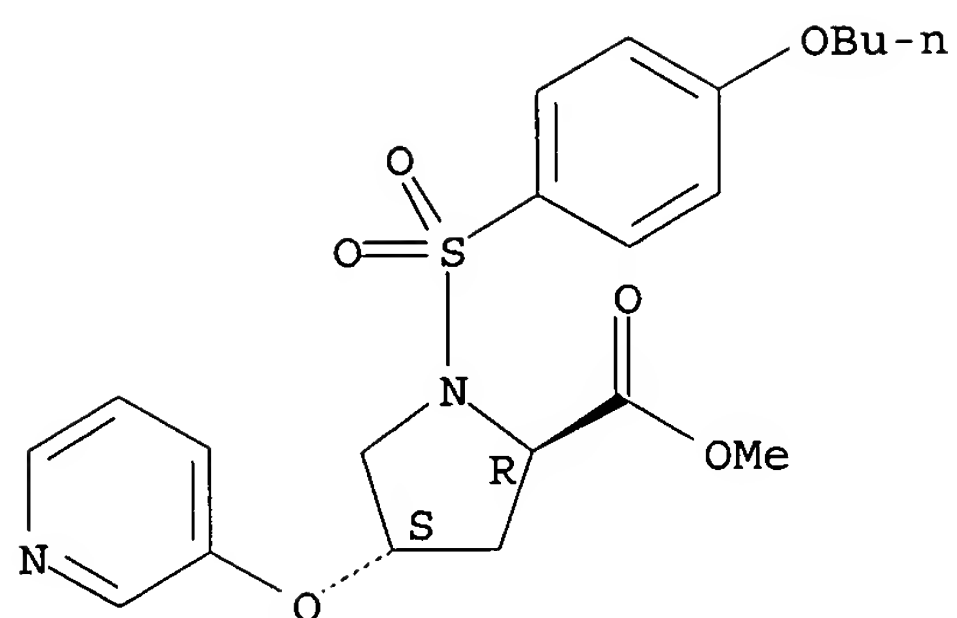
Absolute stereochemistry.



RN 204072-61-7 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(3-pyridinyloxy)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

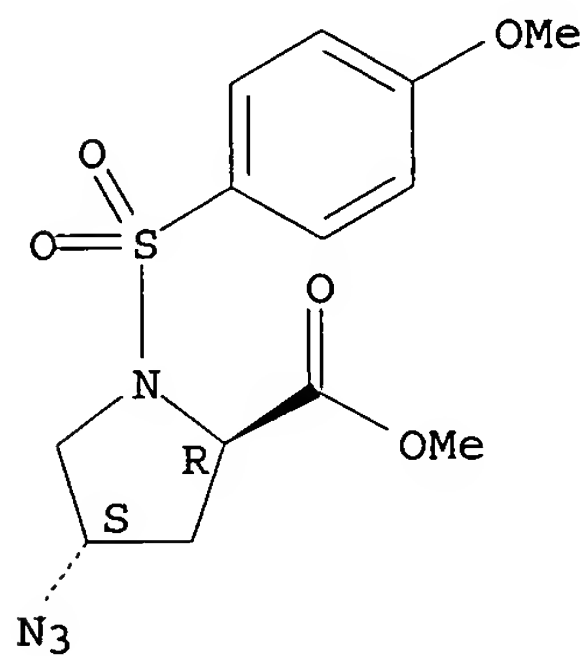
Absolute stereochemistry.



RN 204072-62-8 HCAPLUS

CN D-Proline, 4-azido-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

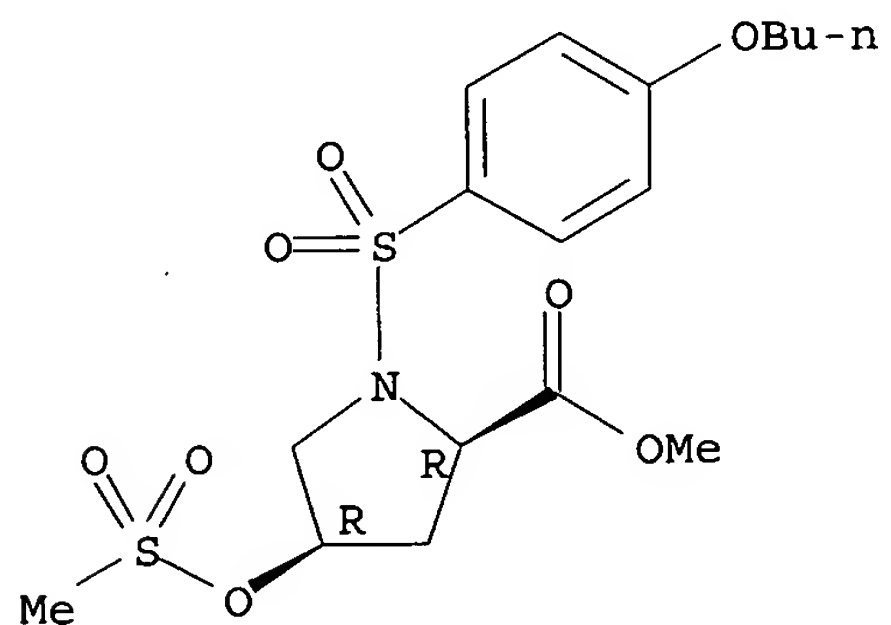
Absolute stereochemistry.



RN 204072-64-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(methylsulfonyl)oxy]-, methyl  
ester, (4R)- (9CI) (CA INDEX NAME)

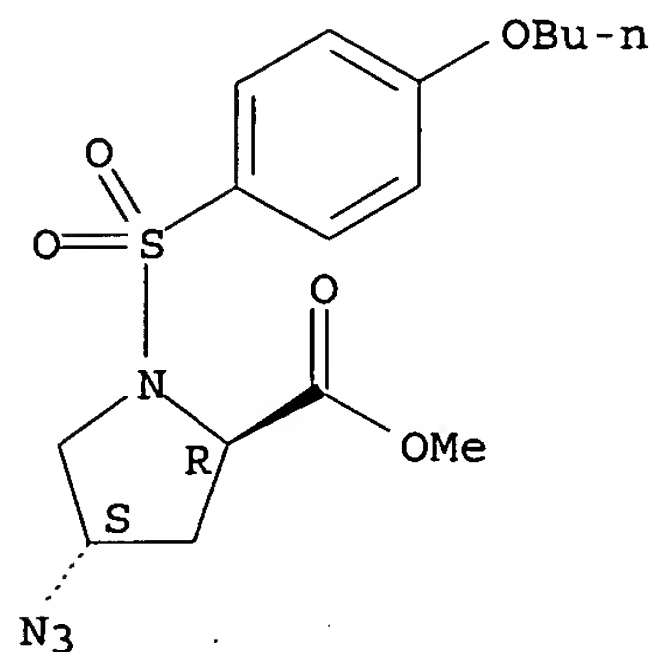
Absolute stereochemistry.



RN 204072-65-1 HCAPLUS

CN D-Proline, 4-azido-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)-  
(9CI) (CA INDEX NAME)

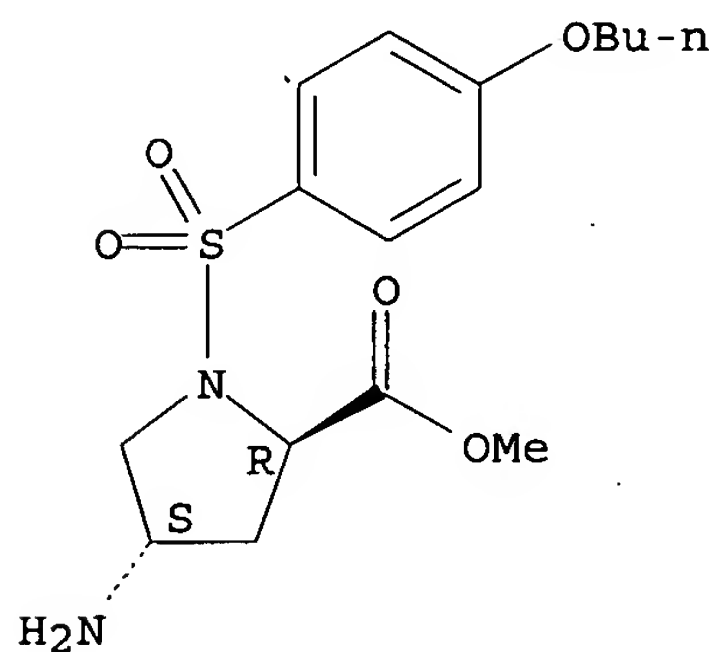
Absolute stereochemistry.



RN 204072-66-2 HCAPLUS

CN D-Proline, 4-amino-1-[(4-butoxyphenyl)sulfonyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

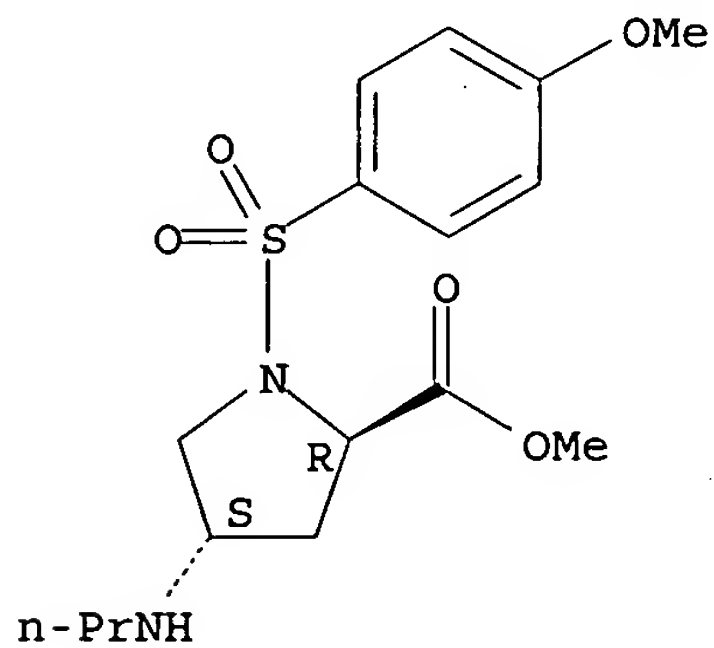
Absolute stereochemistry.



RN 204072-67-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(propylamino)-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

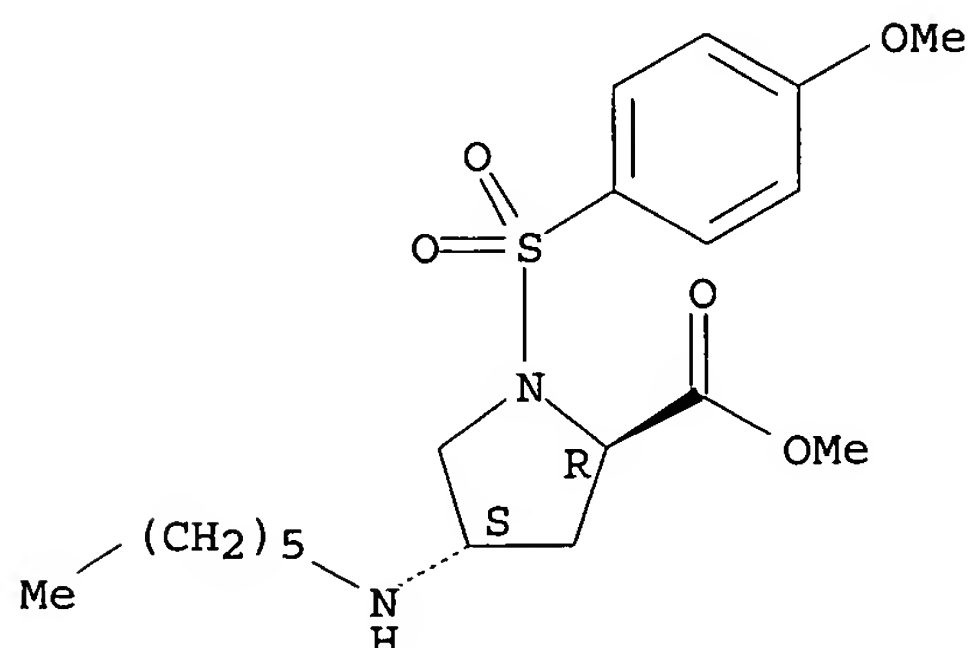


RN 204072-68-4 HCAPLUS

CN D-Proline, 4-(hexylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester,

(4S) - (9CI) (CA INDEX NAME)

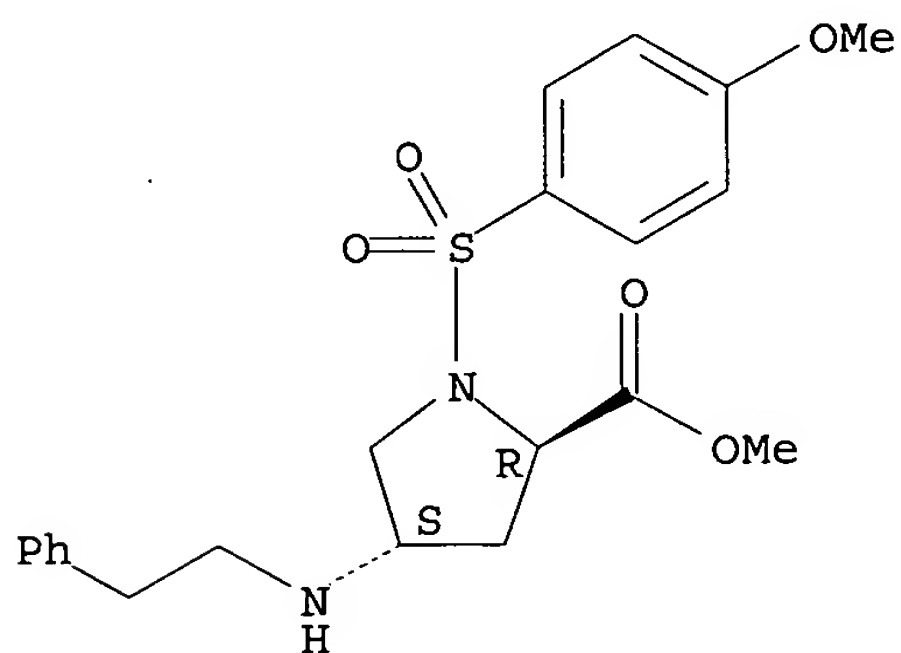
Absolute stereochemistry.



RN 204072-69-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(2-phenylethyl)amino]-, methyl ester, (4S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

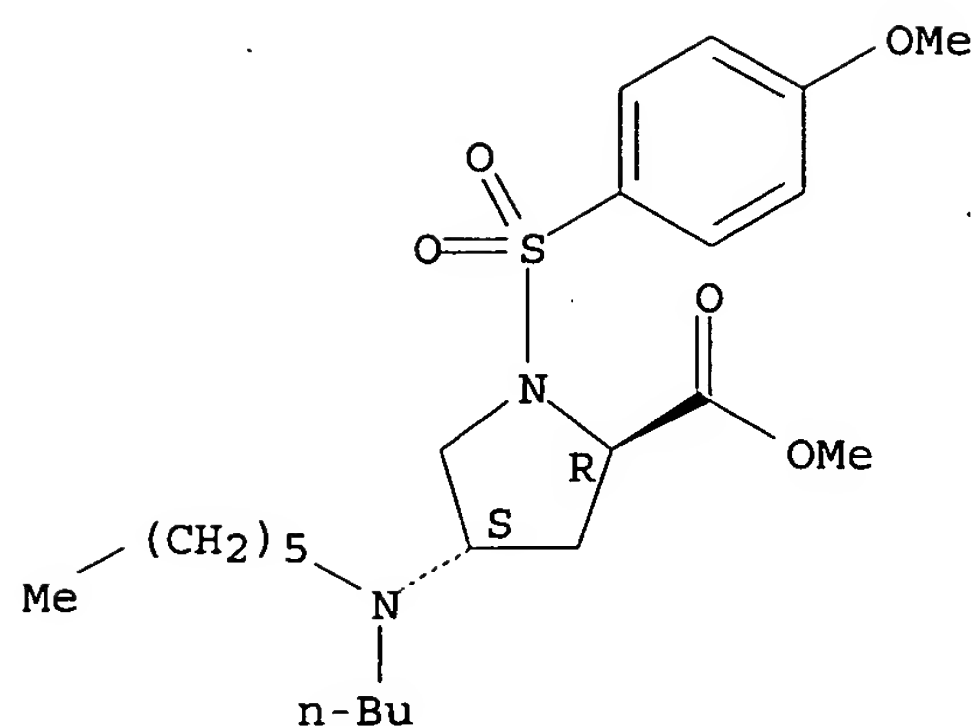


RN 204072-70-8 HCAPLUS

CN D-Proline, 4-(butylhexylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

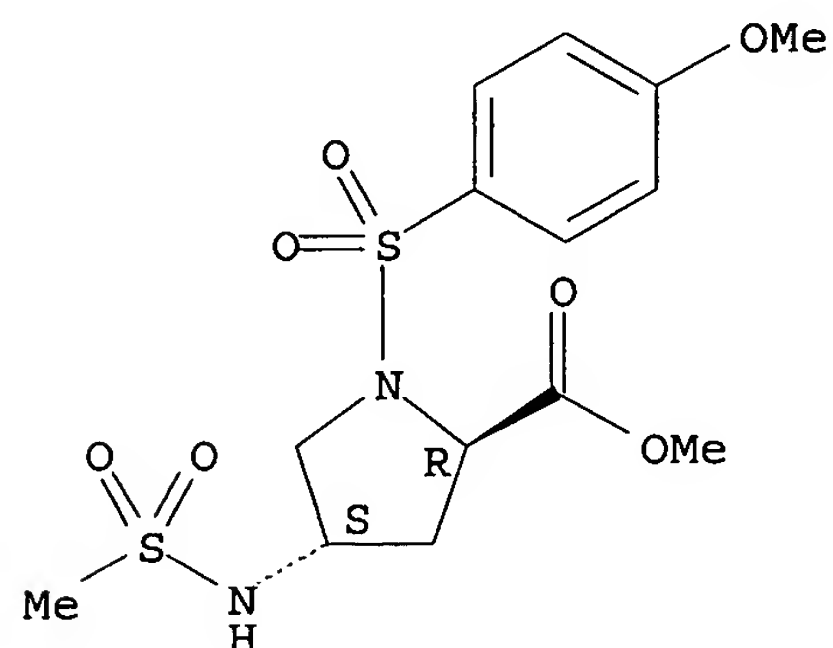




RN 204072-71-9 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methanesulfonyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

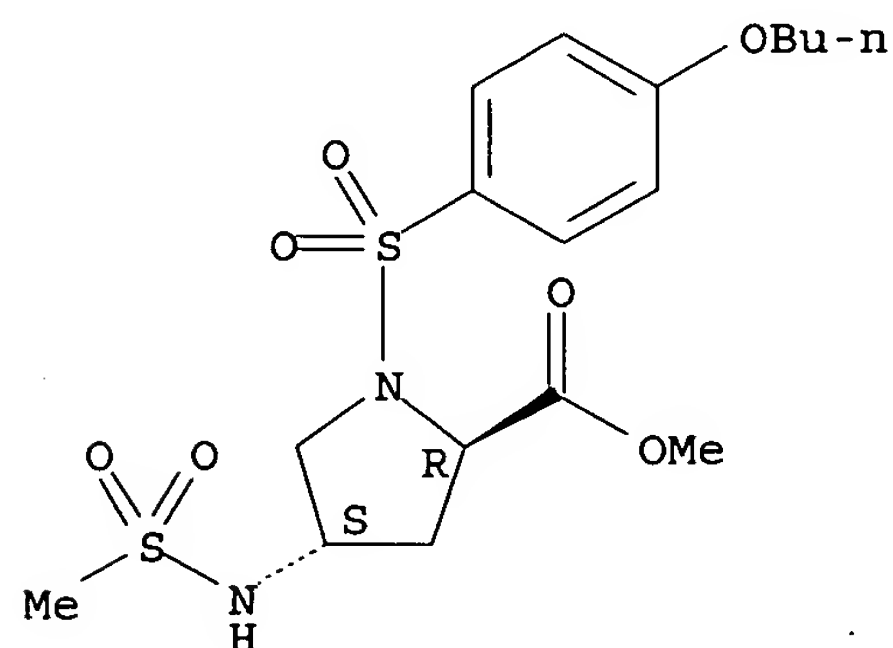
Absolute stereochemistry.



RN 204072-72-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(methanesulfonyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

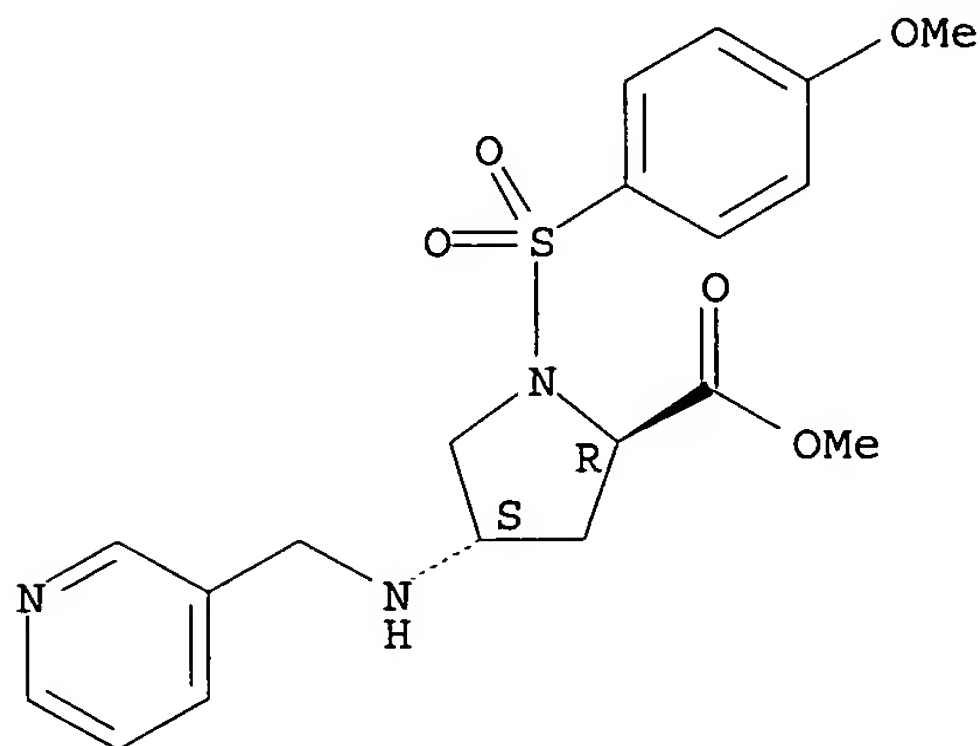
Absolute stereochemistry.



RN 204072-74-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(3-pyridinylmethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

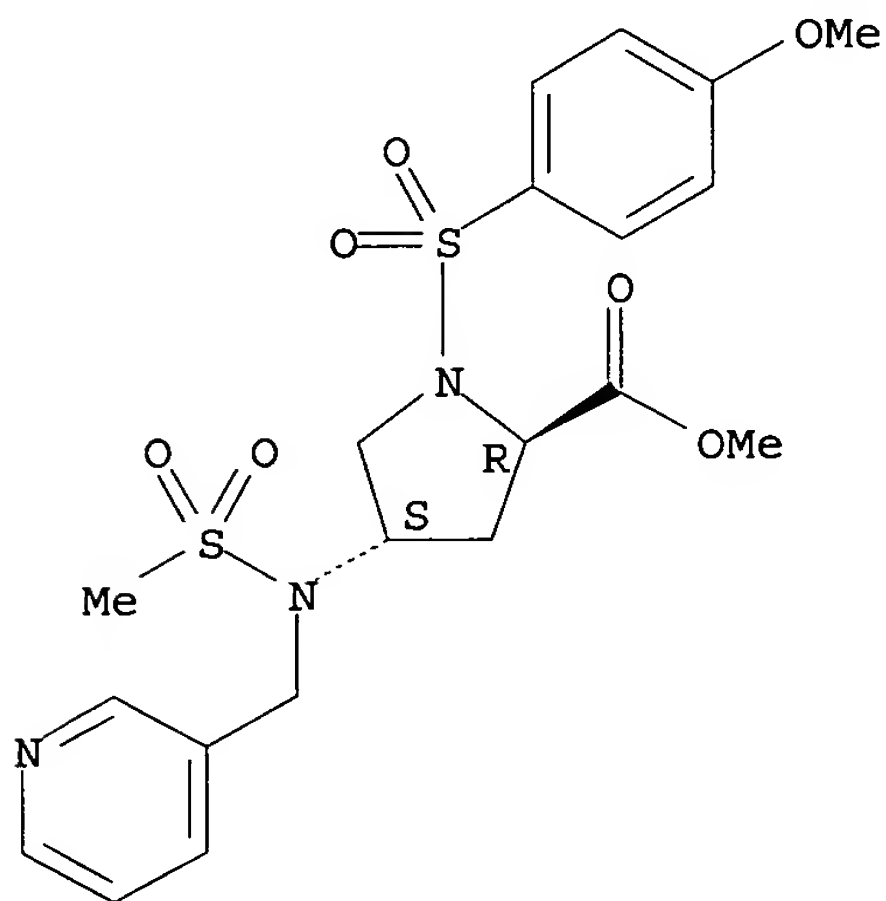
Absolute stereochemistry.



RN 204072-75-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)(3-pyridinylmethyl)amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

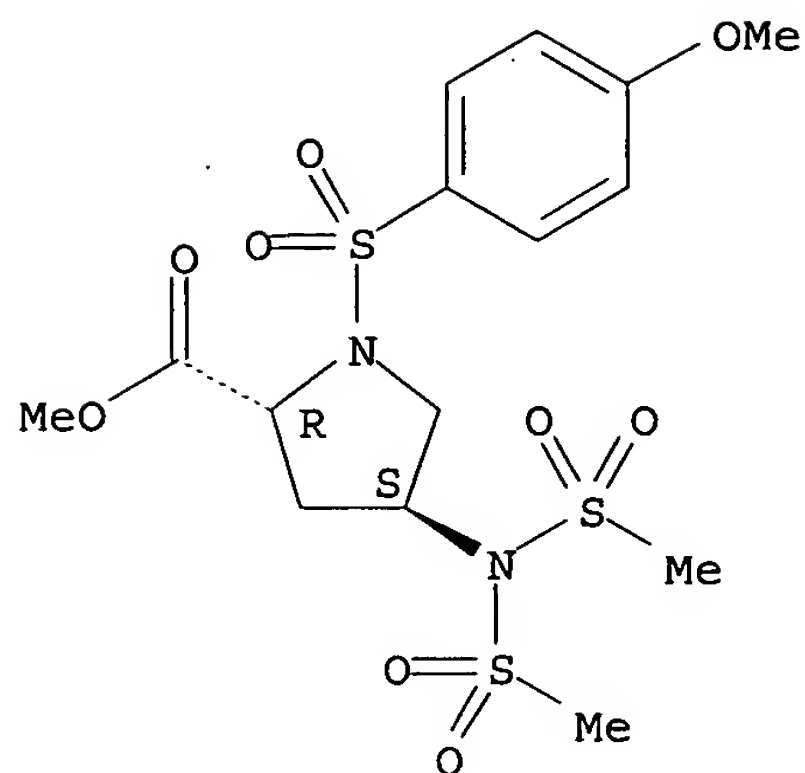
Absolute stereochemistry.



RN 204072-76-4 HCAPLUS

CN D-Proline, 4-[bis(methylsulfonyl)amino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

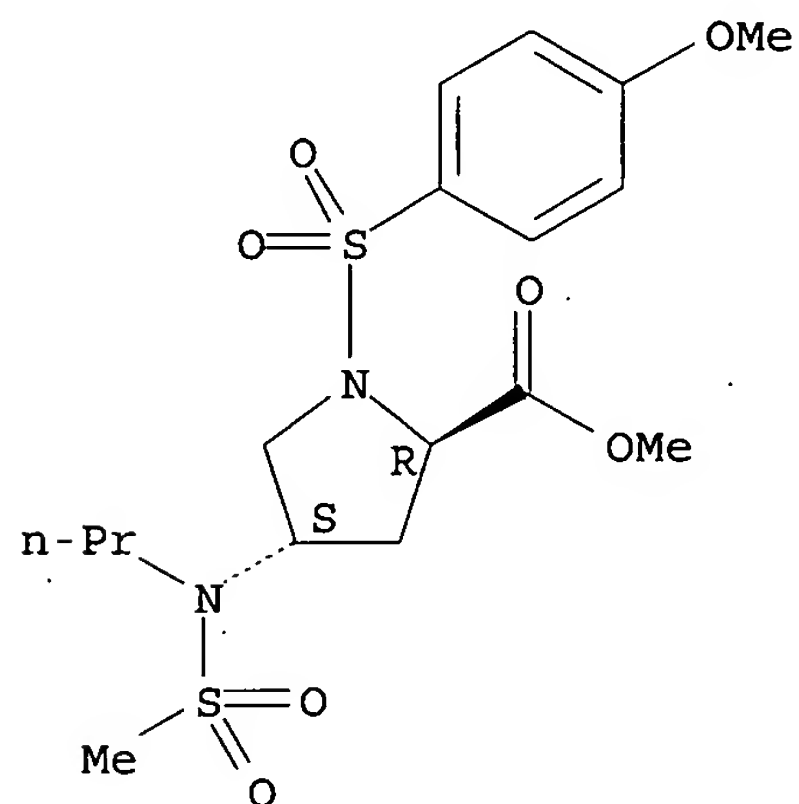
Absolute stereochemistry.



RN 204072-77-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(methylsulfonyl)propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

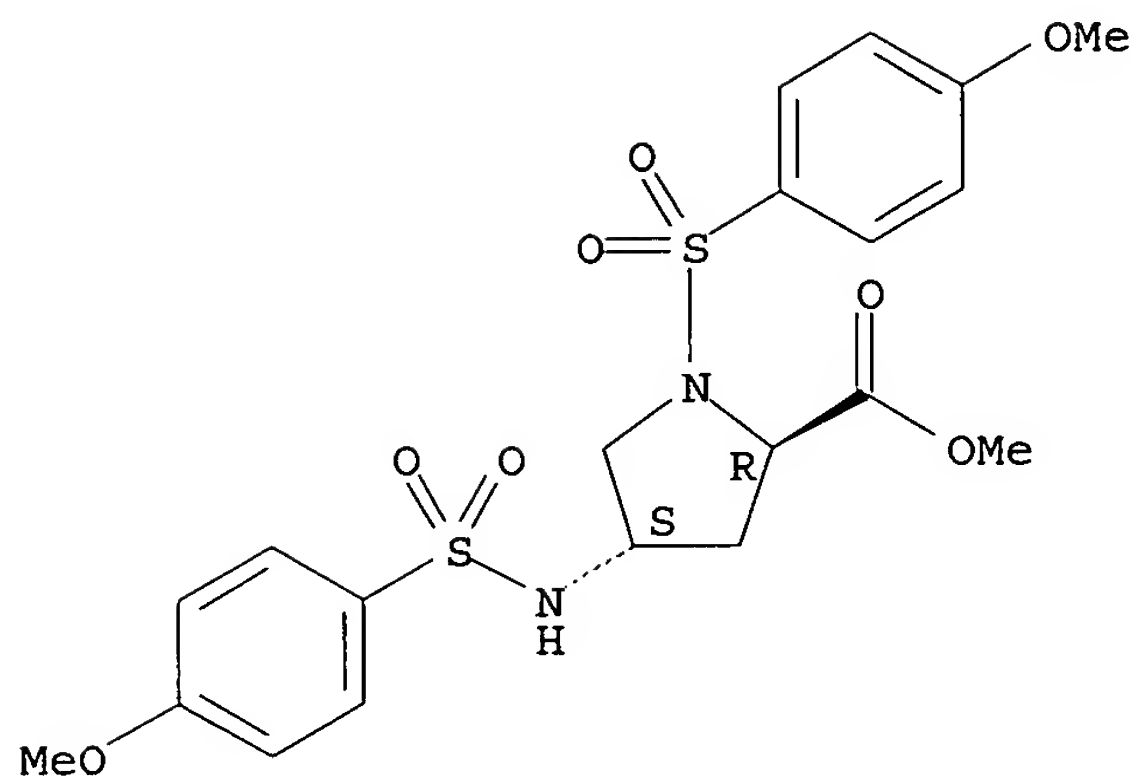
Absolute stereochemistry.



RN 204072-78-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[4-methoxyphenyl)sulfonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

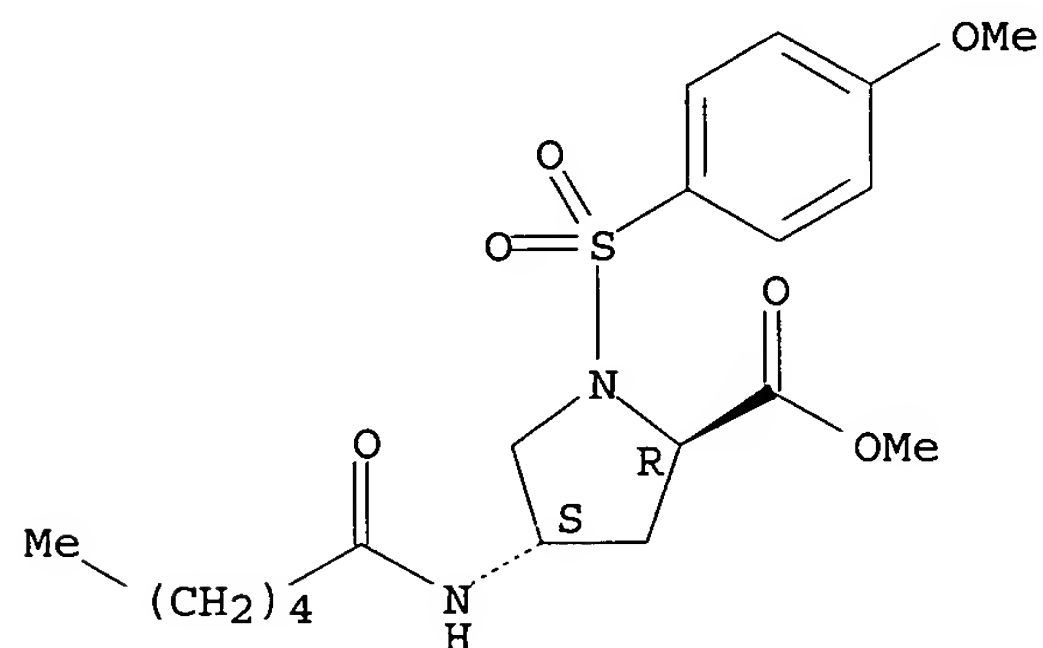
Absolute stereochemistry.



RN 204072-79-7 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[(1-oxohexyl)amino]-, methyl ester, (4S)-(9CI). (CA INDEX NAME)

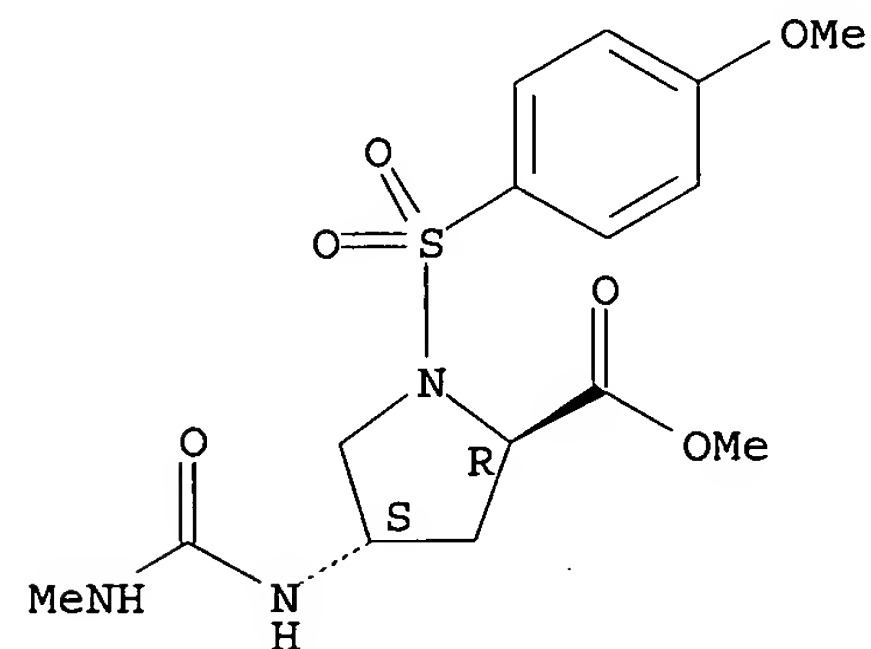
Absolute stereochemistry.



RN 204072-81-1 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[ (methylamino) carbonyl] amino]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

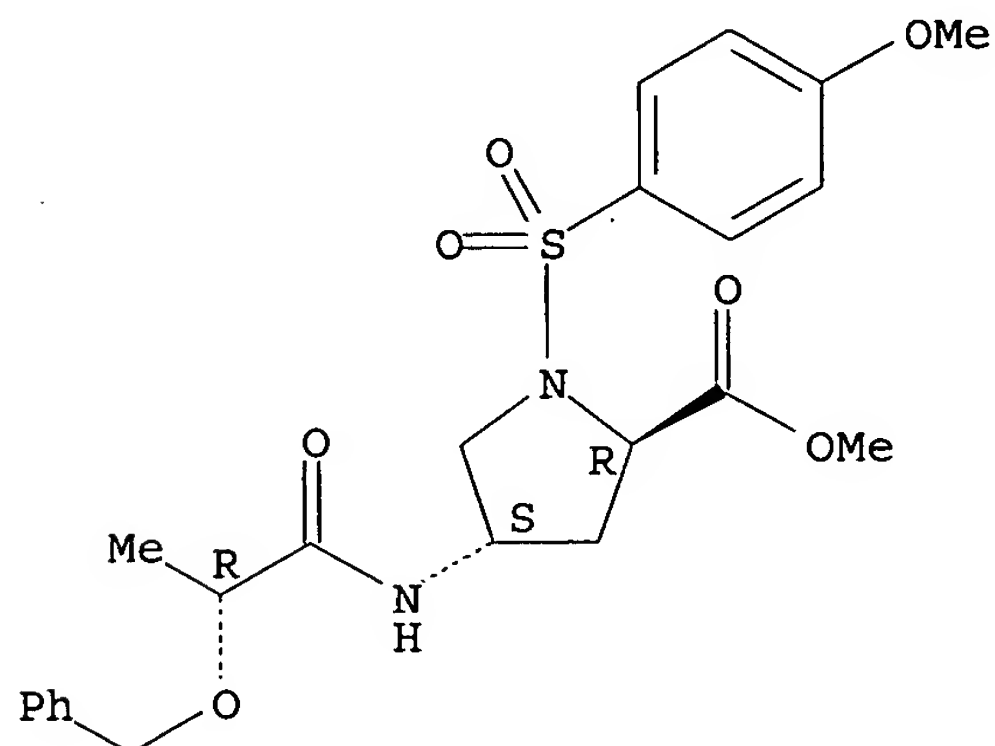
Absolute stereochemistry.



RN 204072-82-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[[(2R)-1-oxo-2-(phenylmethoxy)propyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

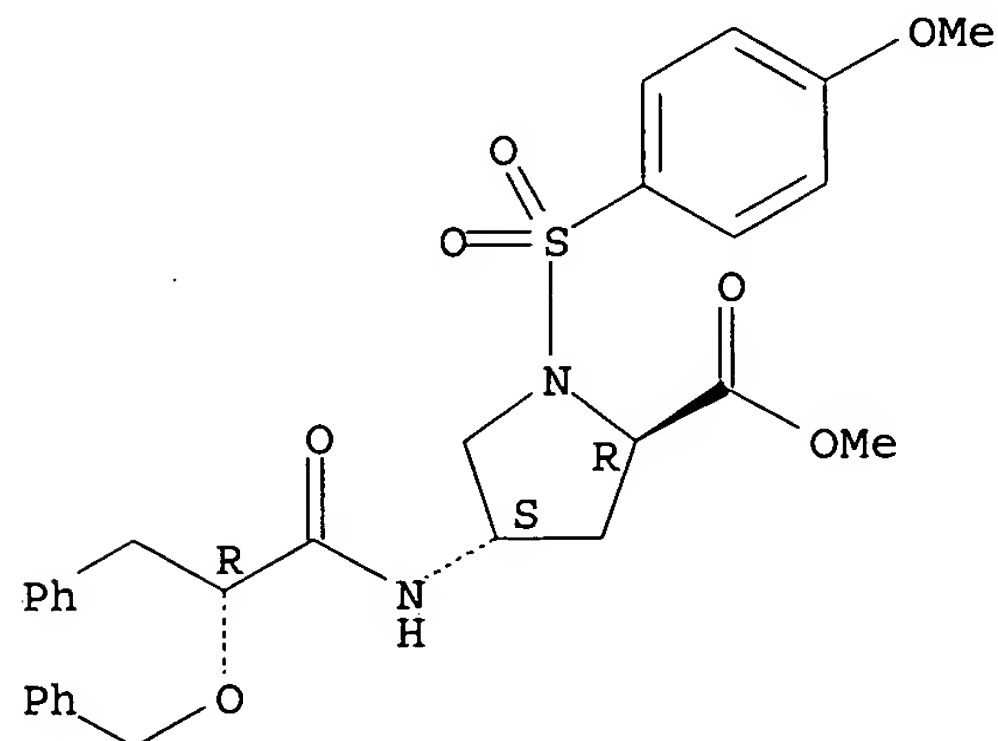
Absolute stereochemistry.



RN 204072-83-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[[(2R)-1-oxo-3-phenyl-2-(phenylmethoxy)propyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

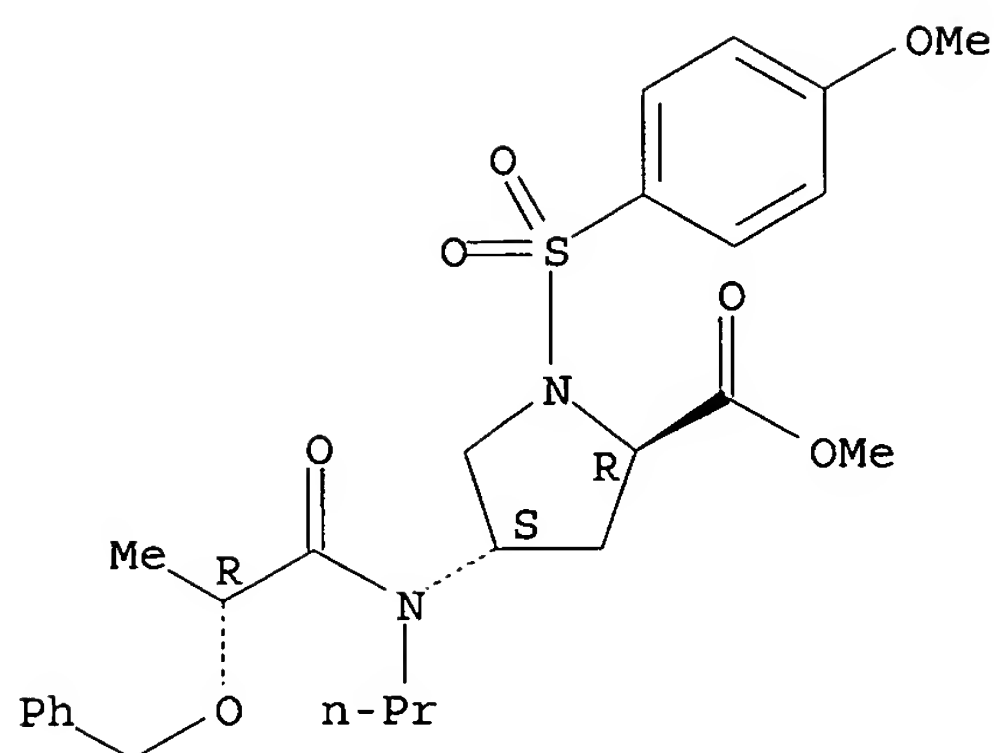
Absolute stereochemistry.



RN 204072-84-4 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[[(2R)-1-oxo-2-(phenylmethoxy)propyl]propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

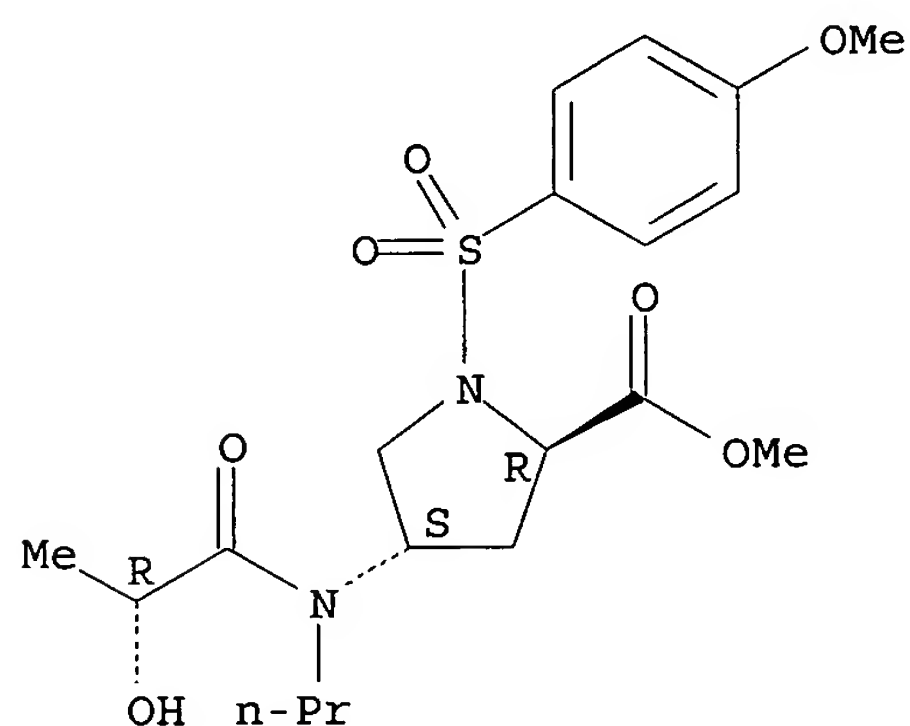
Absolute stereochemistry.



RN 204072-85-5 HCAPLUS

CN D-Proline, 4-[[[(2R)-2-hydroxy-1-oxopropyl]propylamino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

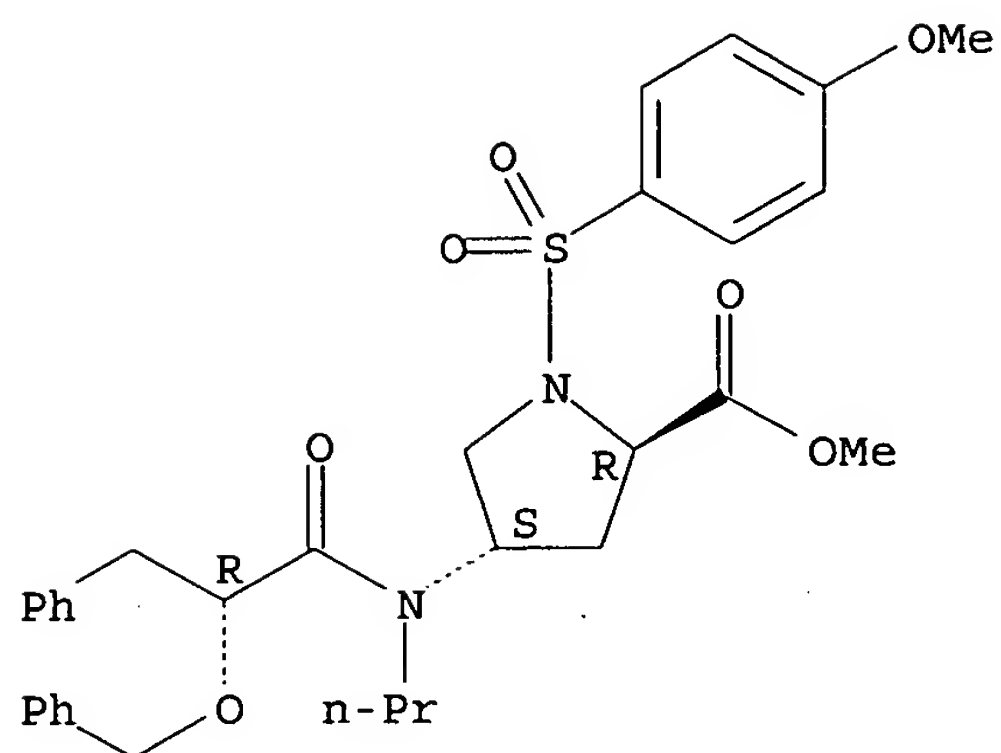
Absolute stereochemistry.



RN 204072-86-6 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[[[(2R)-1-oxo-3-phenyl-2-(phenylmethoxy)propyl]propylamino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

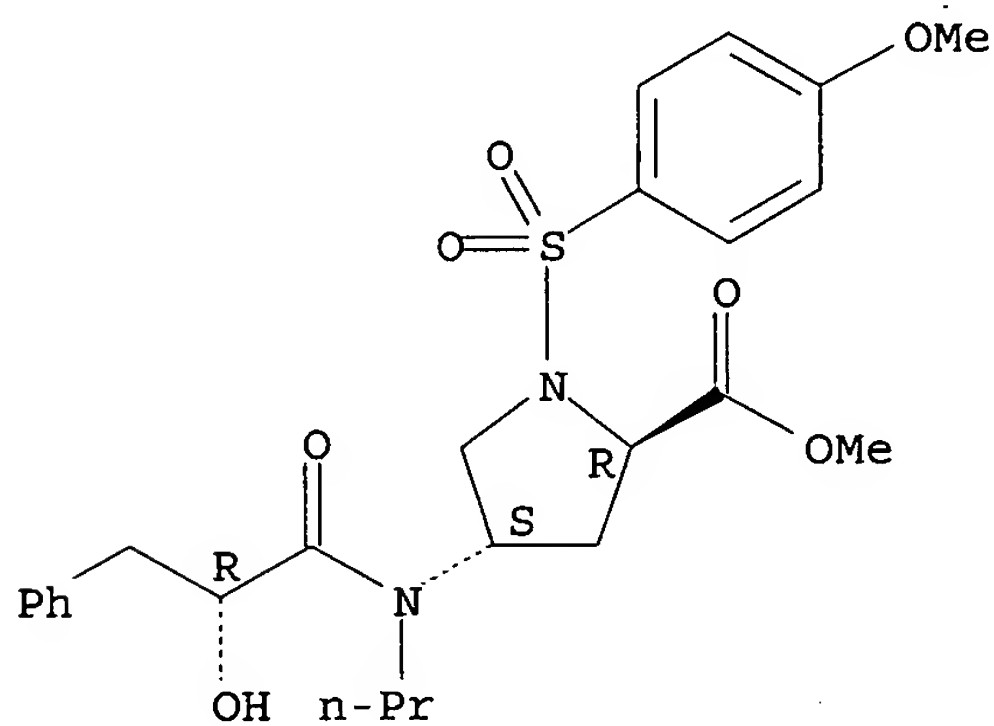
Absolute stereochemistry.



RN 204072-87-7 HCAPLUS

CN D-Proline, 4-[[[(2R)-2-hydroxy-1-oxo-3-phenylpropyl]propylamino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

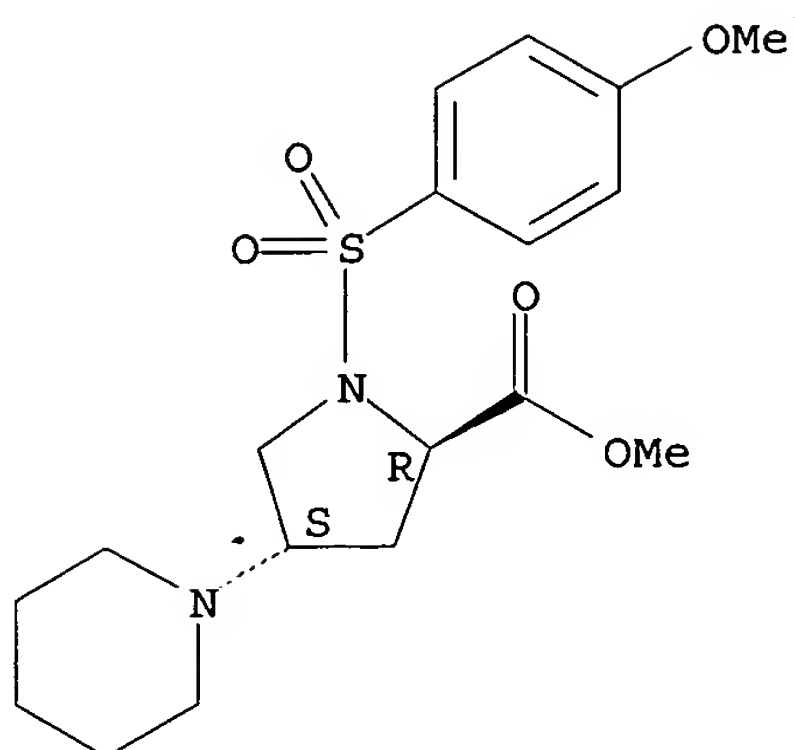
Absolute stereochemistry.



RN 204072-88-8 HCAPLUS

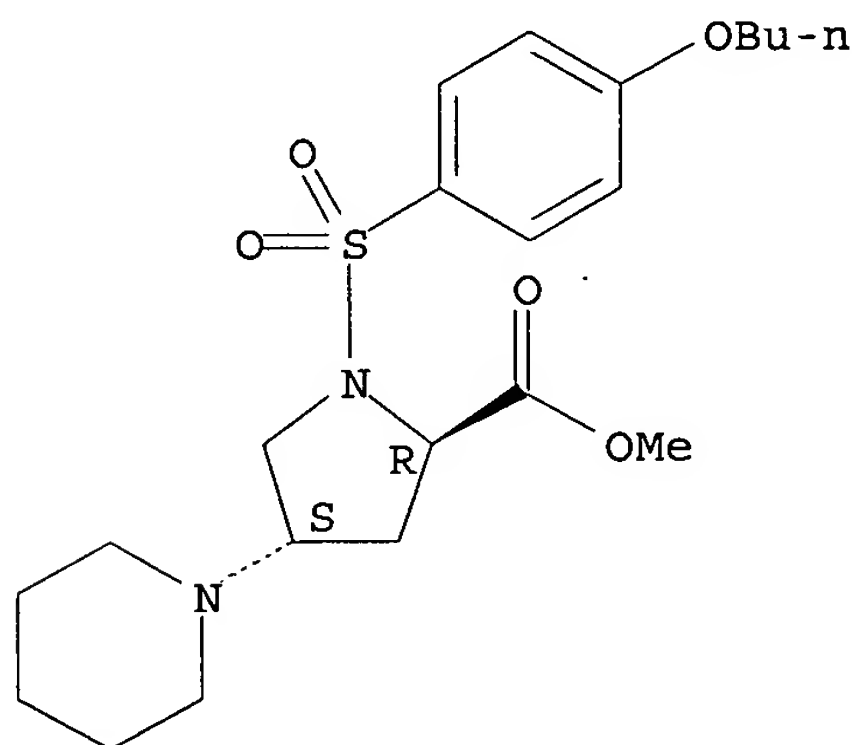
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-89-9 HCAPLUS  
CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, methyl ester,  
(4S)-(9CI) (CA INDEX NAME)

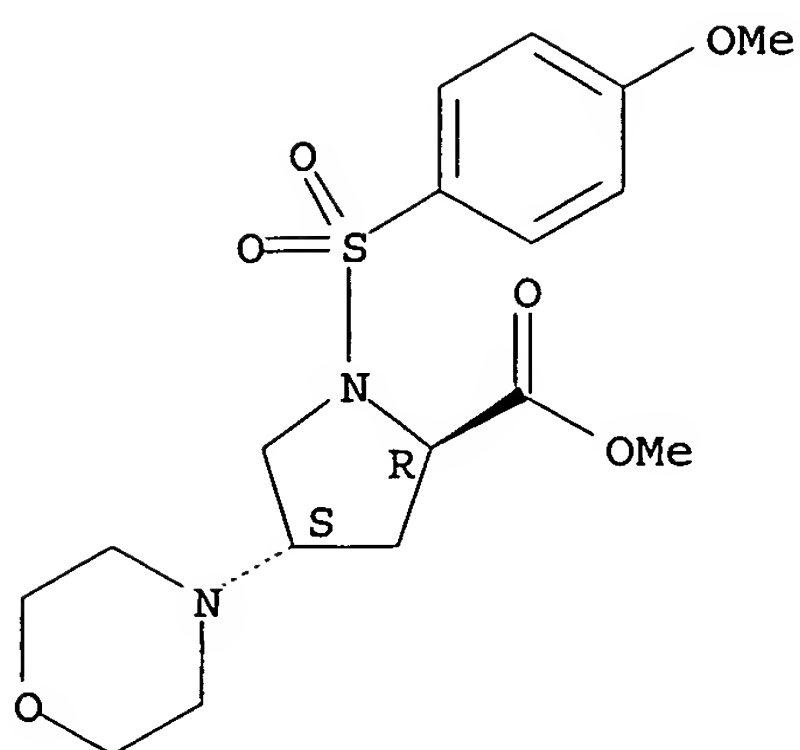
Absolute stereochemistry.



RN 204072-90-2 HCAPLUS  
CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, methyl ester,  
(4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

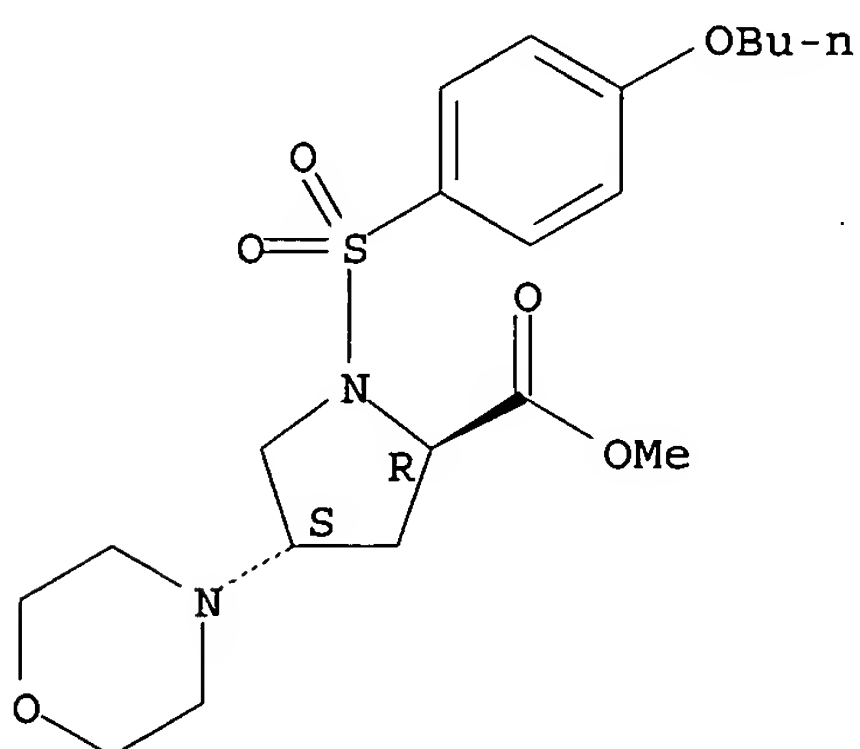




RN 204072-91-3 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, methyl ester,  
(4S)-(9CI) (CA INDEX NAME)

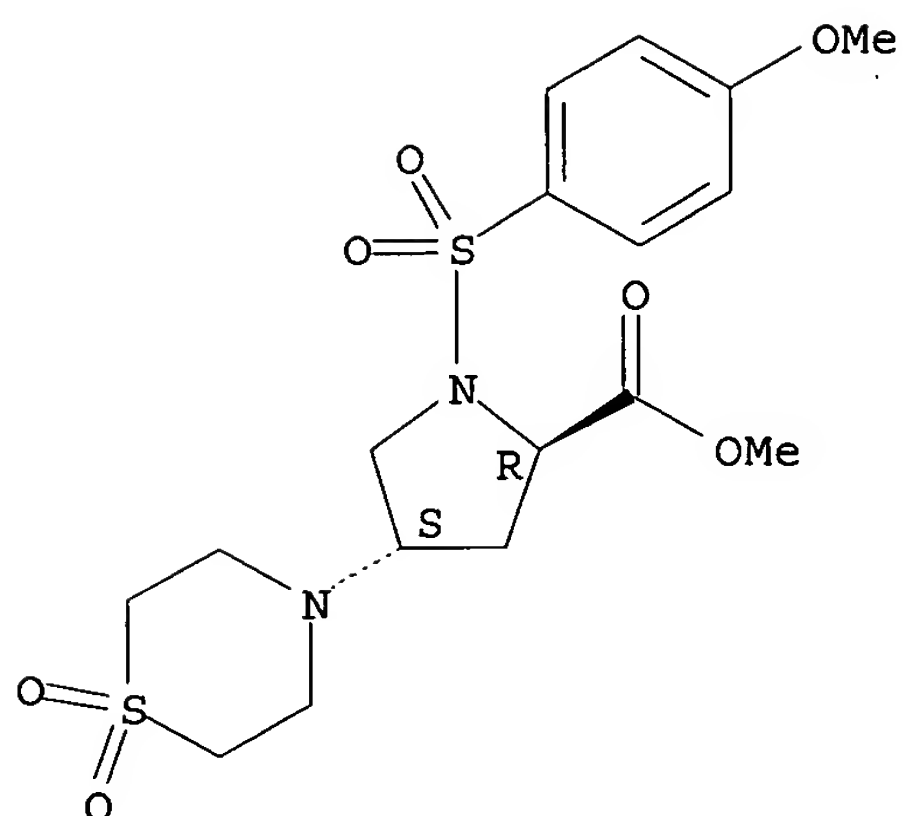
Absolute stereochemistry.



RN 204072-92-4 HCAPLUS

CN D-Proline, 4-(1,1-dioxido-4-thiomorpholinyl)-1-[(4-methoxyphenyl)sulfonyl]-,  
methyl ester, (4S)-(9CI) (CA INDEX NAME)

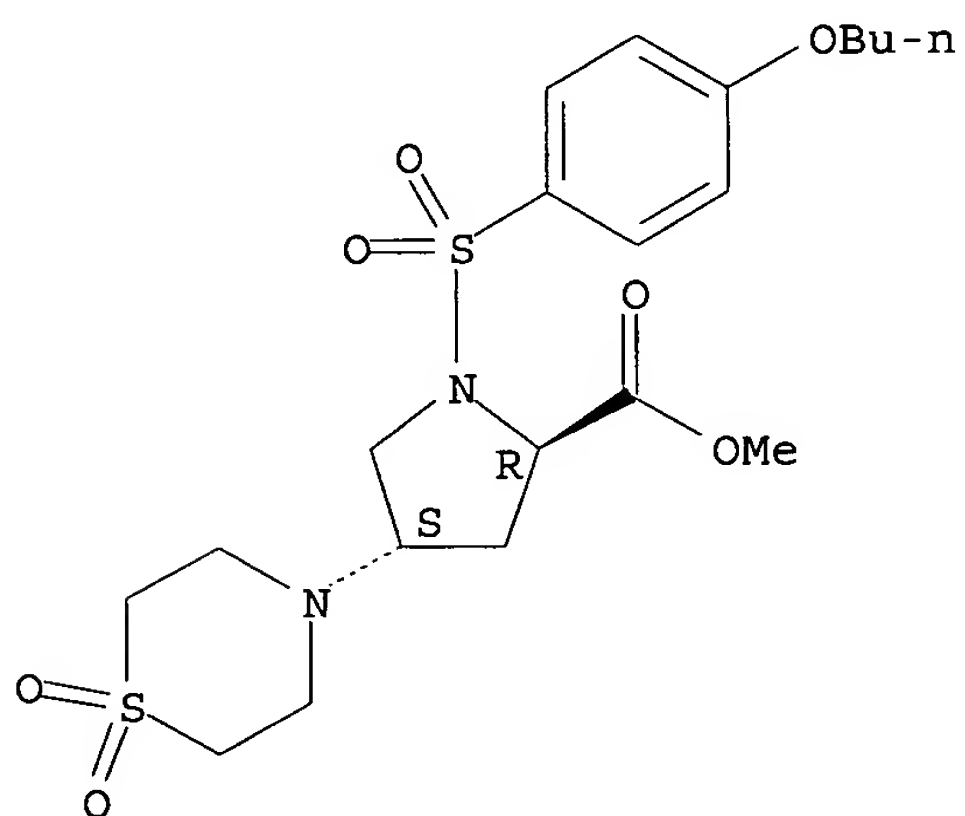
Absolute stereochemistry.



RN 204072-93-5 HCAPLUS

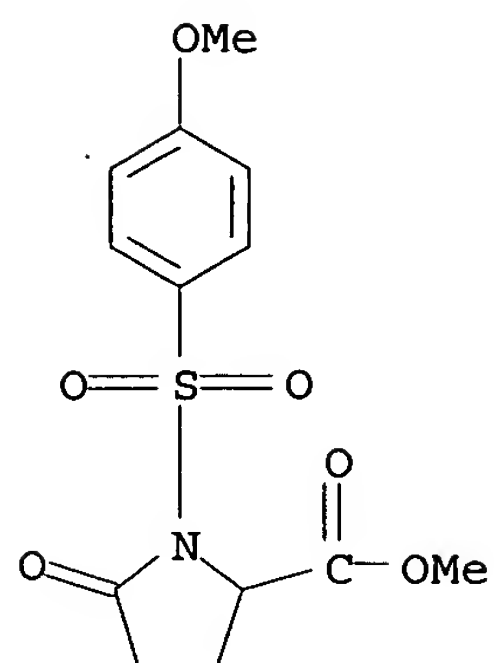
CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(1,1-dioxido-4-thiomorpholinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204073-01-8 HCAPLUS

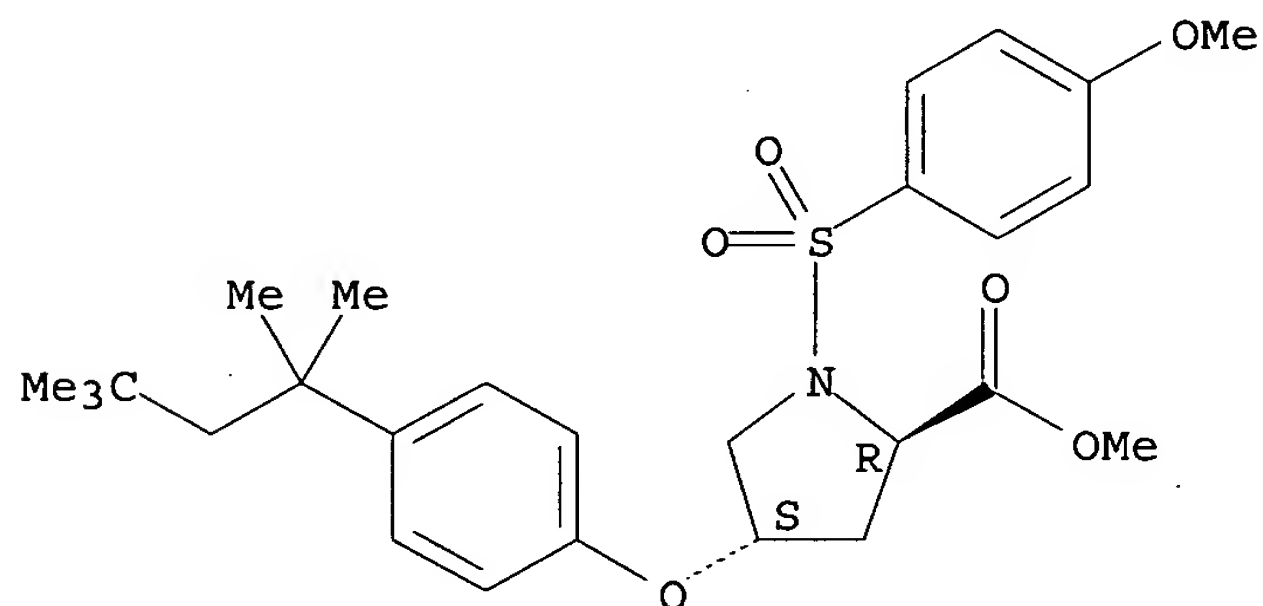
CN Proline, 1-[(4-methoxyphenyl)sulfonyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 537704-28-2 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 537704-31-7 HCAPLUS

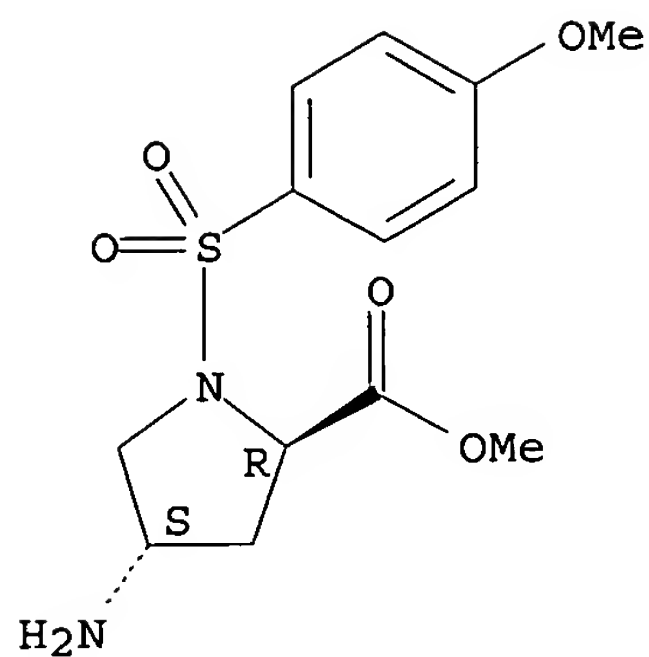
CN D-Proline, 4-amino-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)-, monoformate (9CI) (CA INDEX NAME)

CM 1

CRN 204072-63-9

CMF C13 H18 N2 O5 S

Absolute stereochemistry.



CM 2

CRN 64-18-6

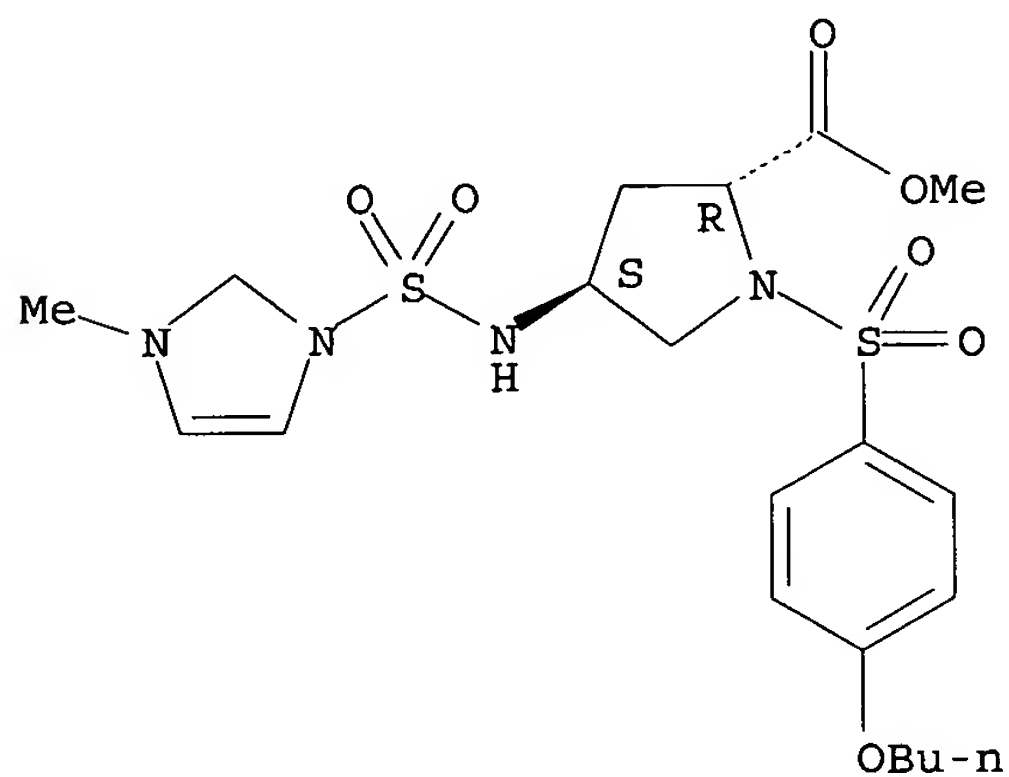
CMF C H2 O2



RN 537704-32-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[[2,3-dihydro-3-methyl-1H-imidazol-1-yl)sulfonyl]amino]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

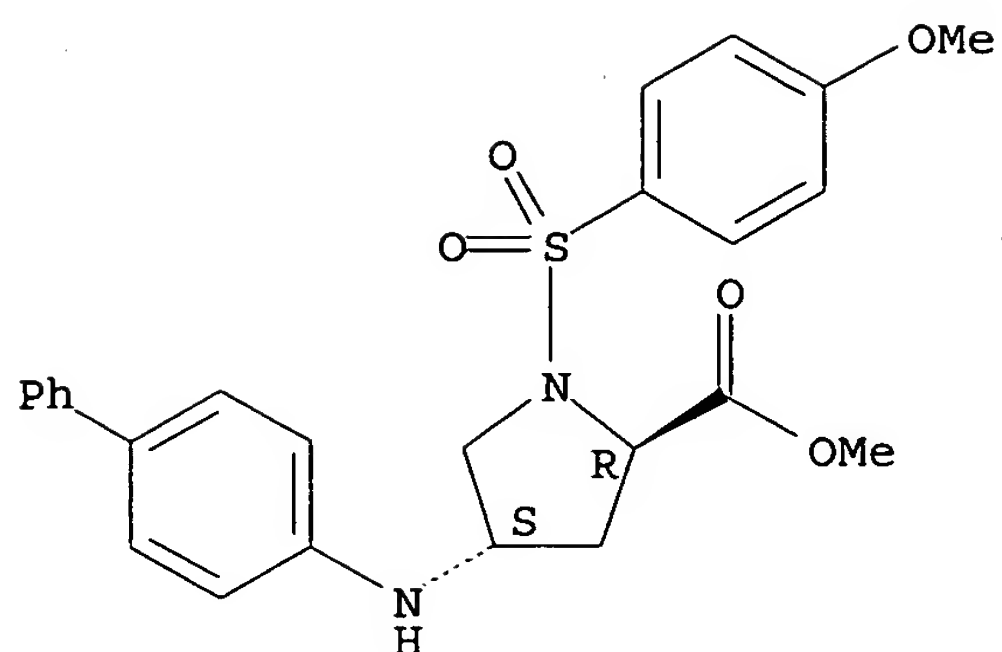
Absolute stereochemistry.



RN 537704-35-1 HCAPLUS

CN D-Proline, 4-([1,1'-biphenyl]-4-ylamino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

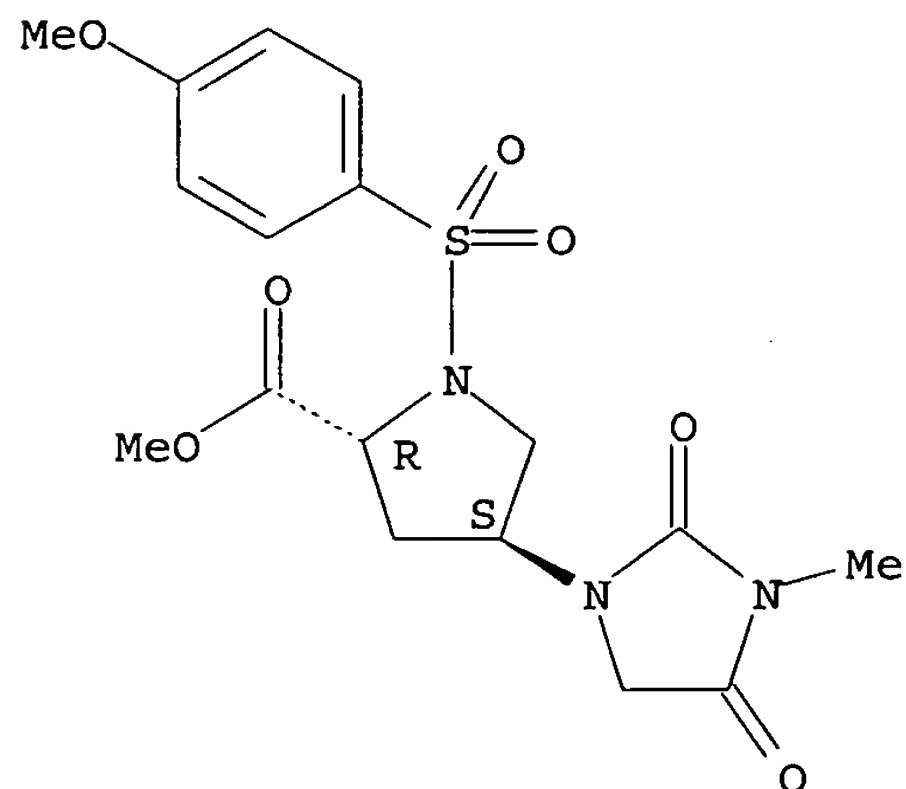
Absolute stereochemistry.



RN 537704-63-5 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

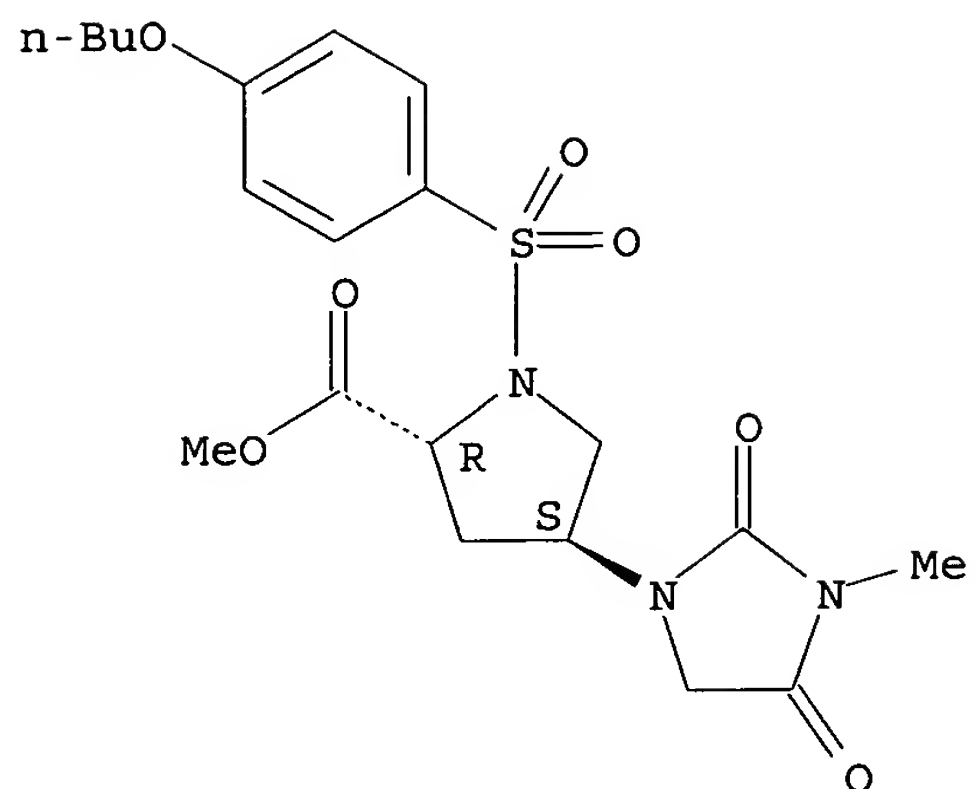
Absolute stereochemistry.



RN 537704-66-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

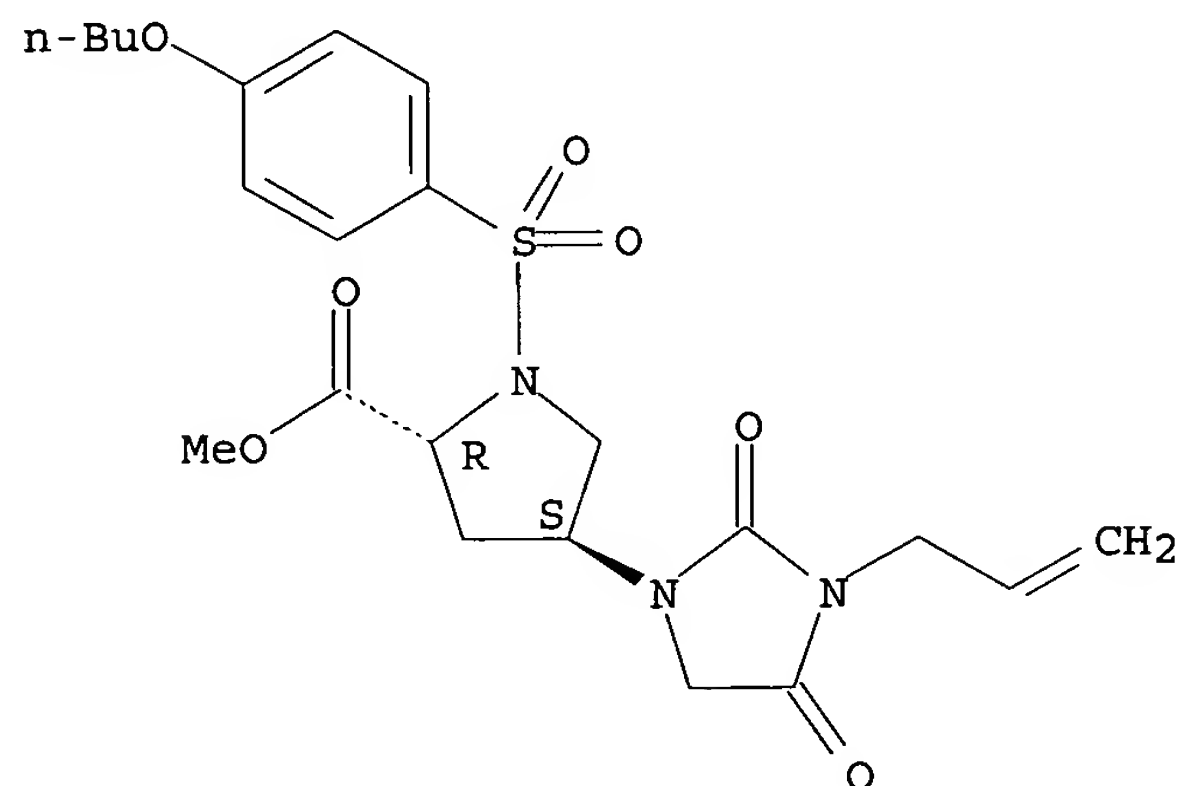
Absolute stereochemistry.



RN 537704-68-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[2,4-dioxo-3-(2-propenyl)-1-imidazolidinyl]-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

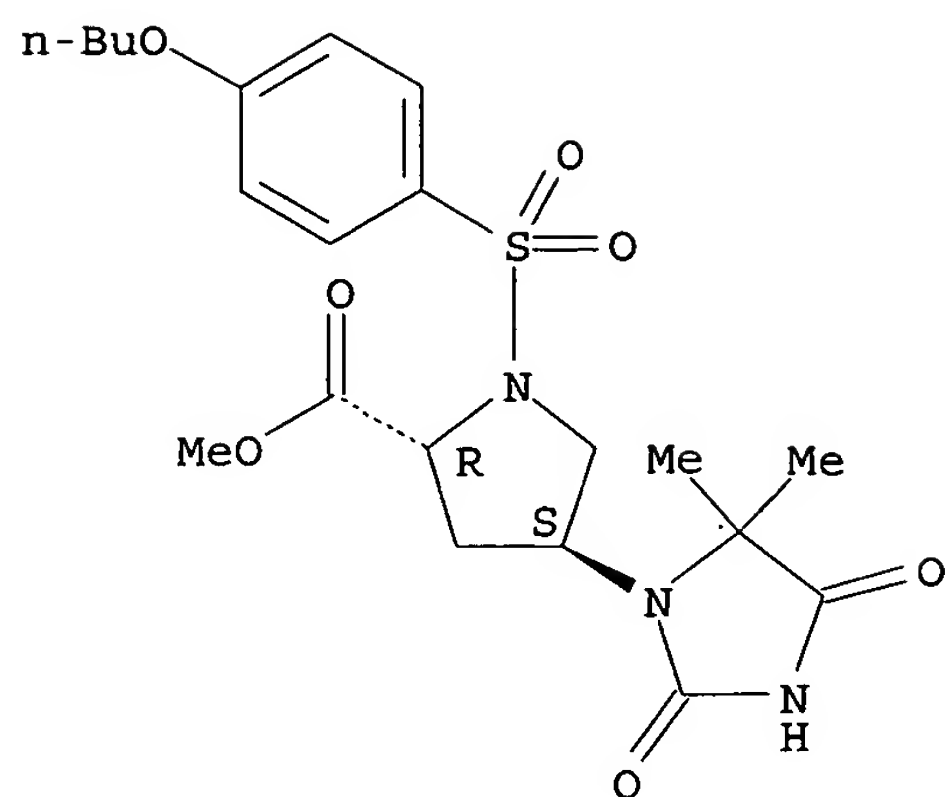
Absolute stereochemistry.



RN 537704-72-6 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(5,5-dimethyl-2,4-dioxo-1-imidazolidinyl)-, methyl ester, (4S)-(9CI) (CA INDEX NAME)

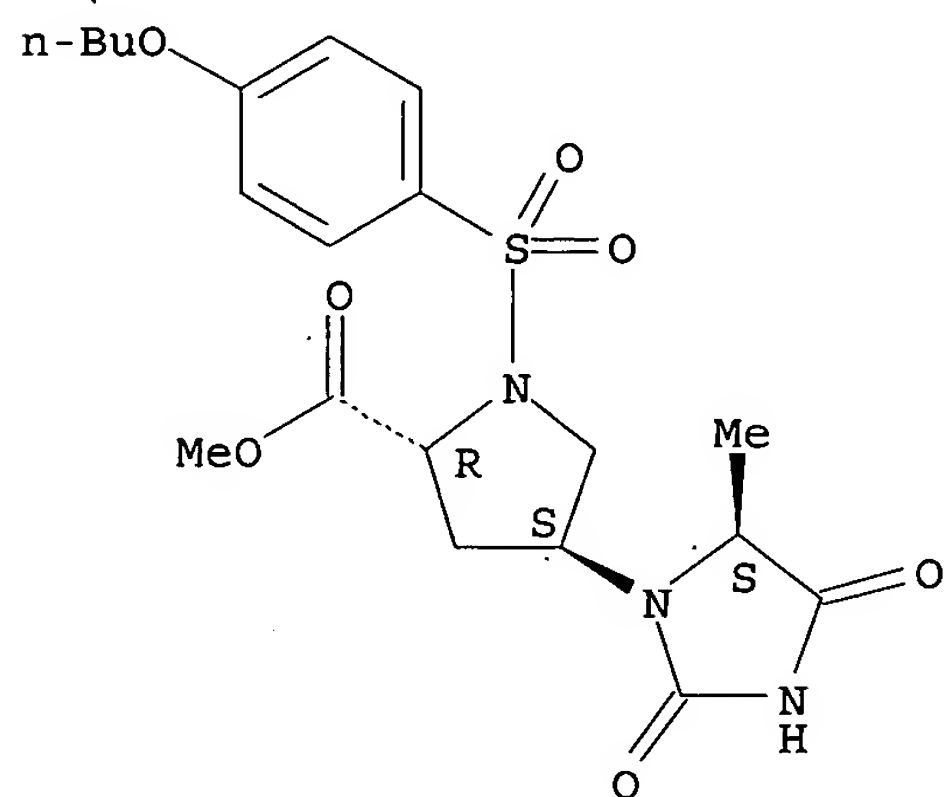
Absolute stereochemistry.



RN 537704-74-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(5S)-5-methyl-2,4-dioxo-1-imidazolidinyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

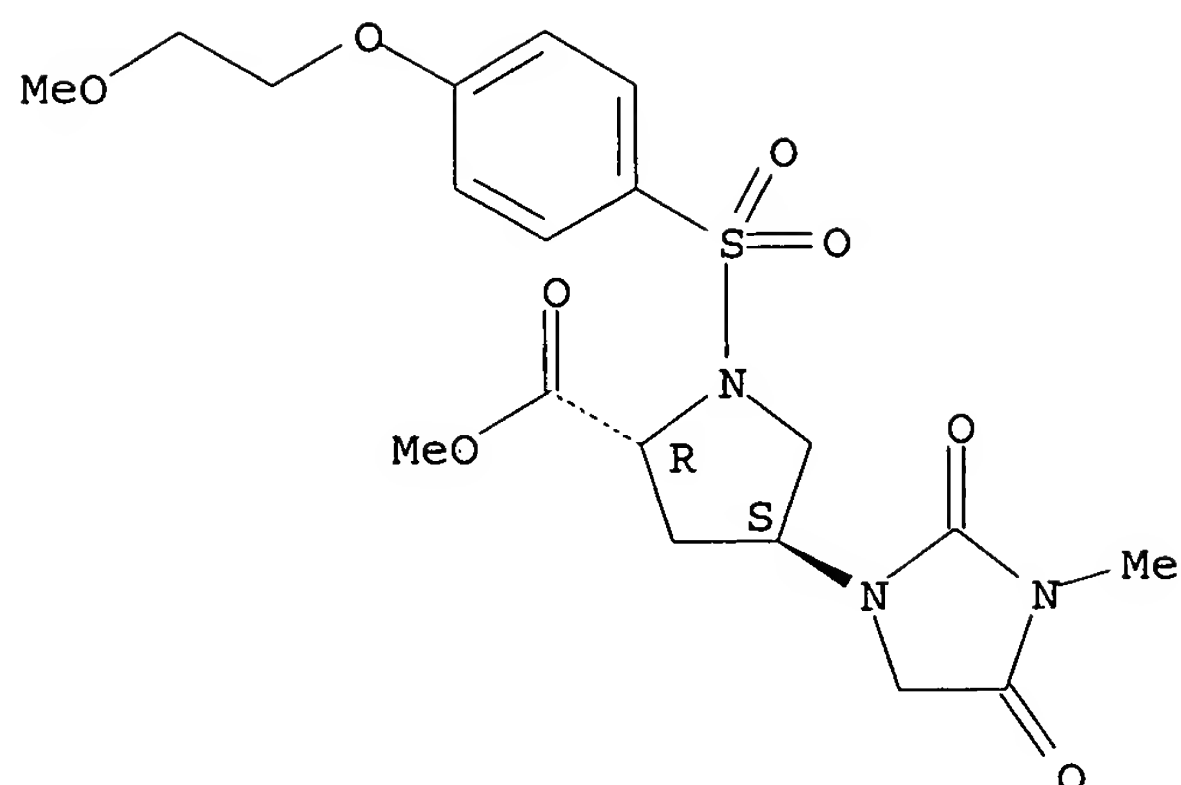
Absolute stereochemistry.



RN 537704-76-0 HCAPLUS

CN D-Proline, 1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

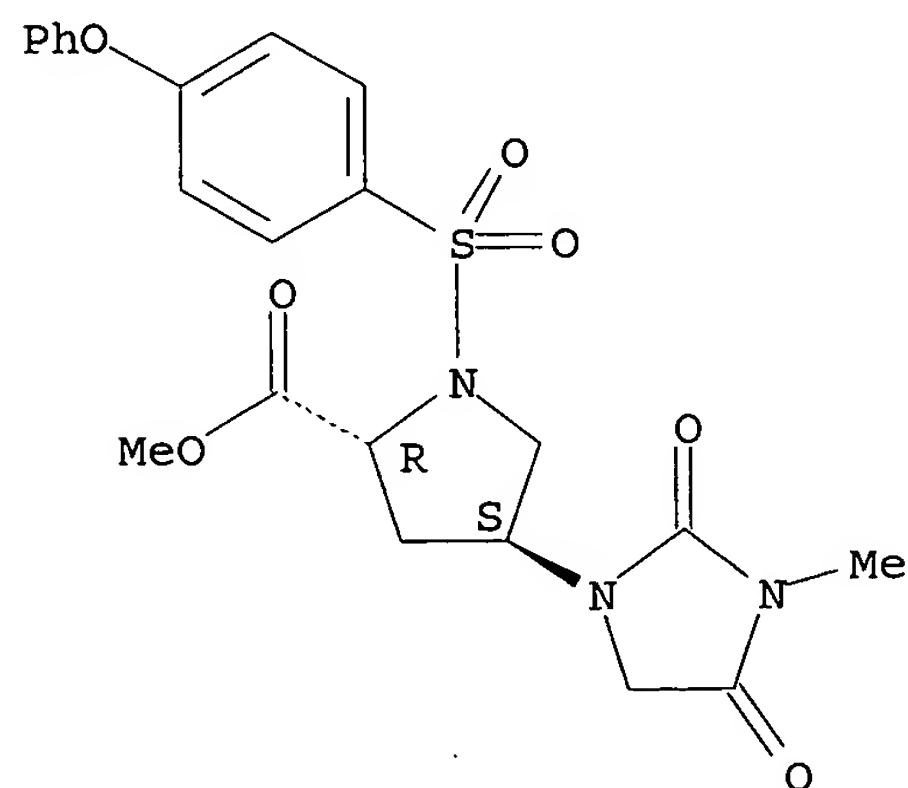
Absolute stereochemistry.



RN 537704-78-2 HCAPLUS

CN D-Proline, 4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 204071-58-9P 204071-59-0P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-4-hydroxy-4-ethylpyrrolidine  
 204071-60-3P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4R)-4-hydroxy-4-phenylpyrrolidine  
 204071-62-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-3,3-dimethyl-(4R)-hydroxypyrrolidine  
 204071-99-8P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-piperidyl)pyrrolidine 204072-00-4P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1-piperidyl)pyrrolidine 204072-01-5P, N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-morpholinopyrrolidine  
 204072-02-6P, N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-morpholinopyrrolidine 204072-03-7P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 204072-04-8P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(1,1-dioxothiomorpholino)pyrrolidine 537704-65-7P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-67-9P,



N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1-methylimidazolidin-3-yl)pyrrolidine 537704-69-1P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,5-dioxo-1-allylimidazolidin-3-yl)pyrrolidine 537704-73-7P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(2,4-dioxo-5,5-dimethylimidazolidin-1-yl)pyrrolidine 537704-75-9P,  
 N-(4-Butoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-[(5S)-5-methyl-2,4-dioxoimidazolidin-1-yl]pyrrolidine 537704-77-1P,  
 N-[4-(2-Methoxyethoxy)phenylsulfonyl]-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-79-3P,  
 N-(4-Phenoxyphenylsulfonyl)-(2R)-(N-hydroxycarboxamido)-(4S)-(3-methyl-2,4-dioxoimidazolidin-1-yl)pyrrolidine 537704-80-6P,  
 N-(4-Methoxyphenylsulfonyl)-(2R)-hydroxycarboxamido-(4R)-4-hydroxy-4-ethylpyrrolidine

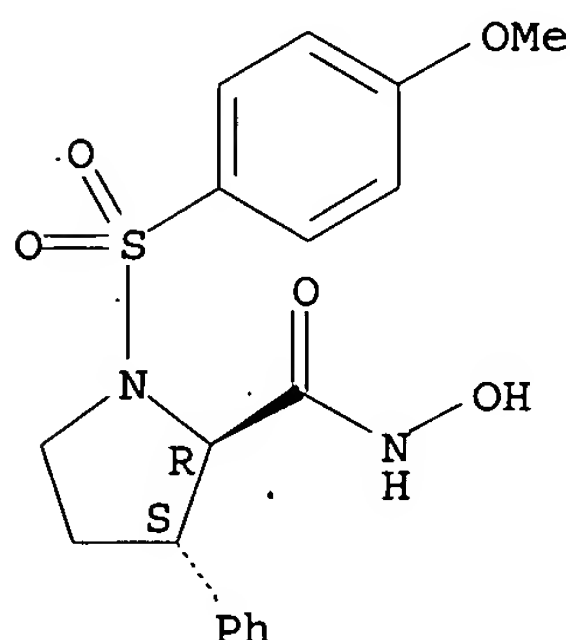
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted cyclic amines as metalloprotease inhibitors for treating conditions characterized by excess activity of these enzymes)

RN 204071-58-9 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-3-phenyl-, (2R,3S)-rel- (9CI) (CA INDEX NAME)

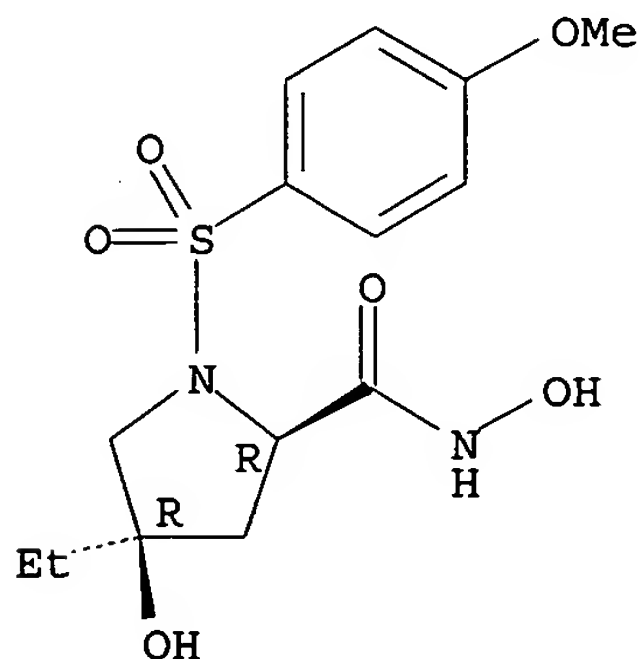
Relative stereochemistry.



RN 204071-59-0 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 4-ethyl-N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (2R,4R)- (9CI) (CA INDEX NAME)

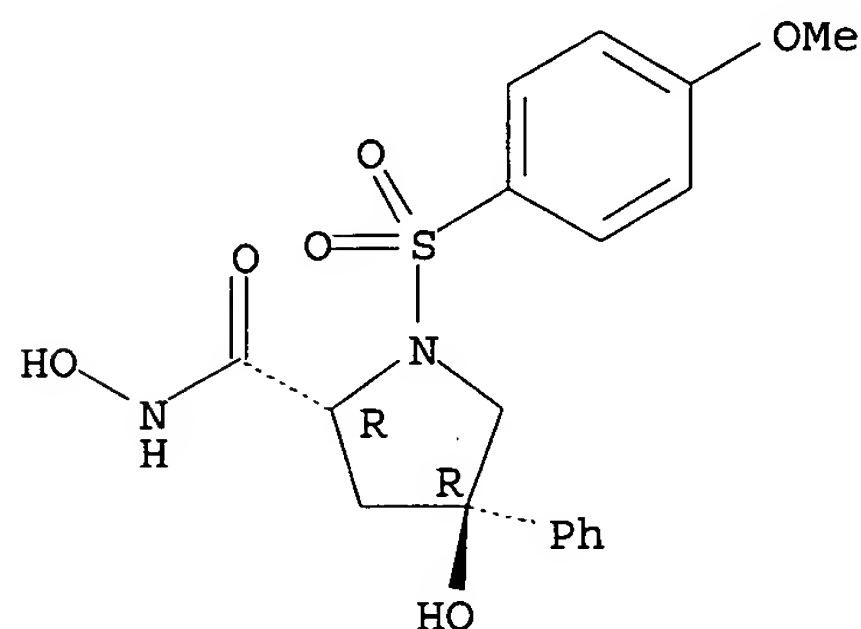
Absolute stereochemistry.



RN 204071-60-3 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-phenyl-, (2R,4R)- (9CI) (CA INDEX NAME)

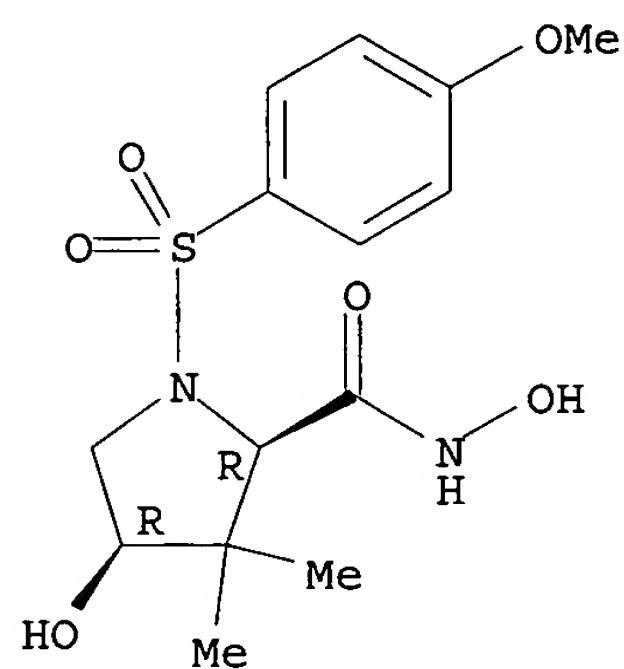
Absolute stereochemistry.



RN 204071-62-5 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N,4-dihydroxy-1-[(4-methoxyphenyl)sulfonyl]-3,3-dimethyl-, (2R,4R)- (9CI) (CA INDEX NAME)

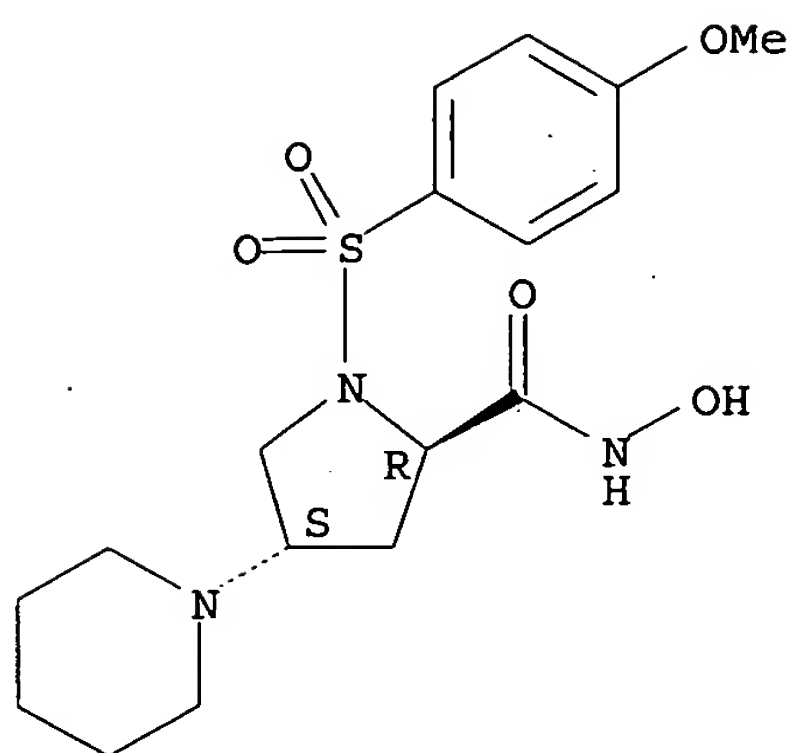
Absolute stereochemistry.



RN 204071-99-8 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(1-piperidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

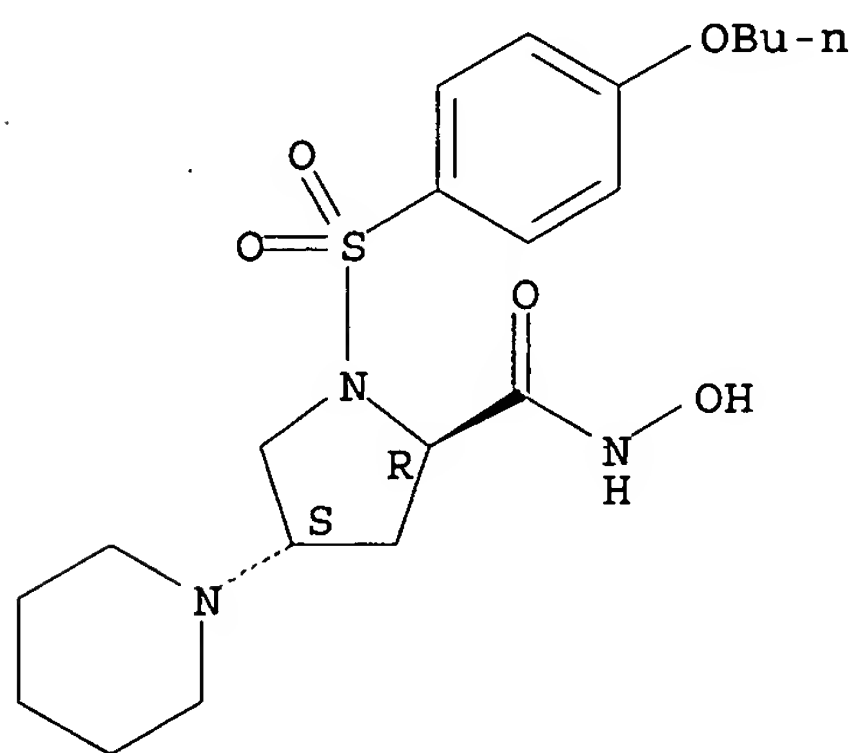
Absolute stereochemistry.



RN 204072-00-4 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(1-piperidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

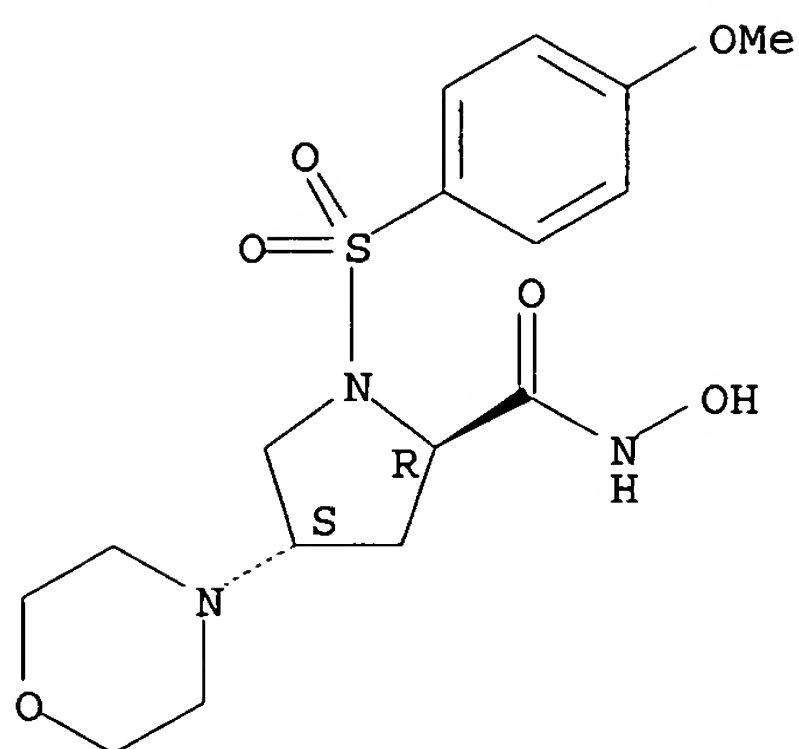
Absolute stereochemistry.



RN 204072-01-5 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(4-morpholinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

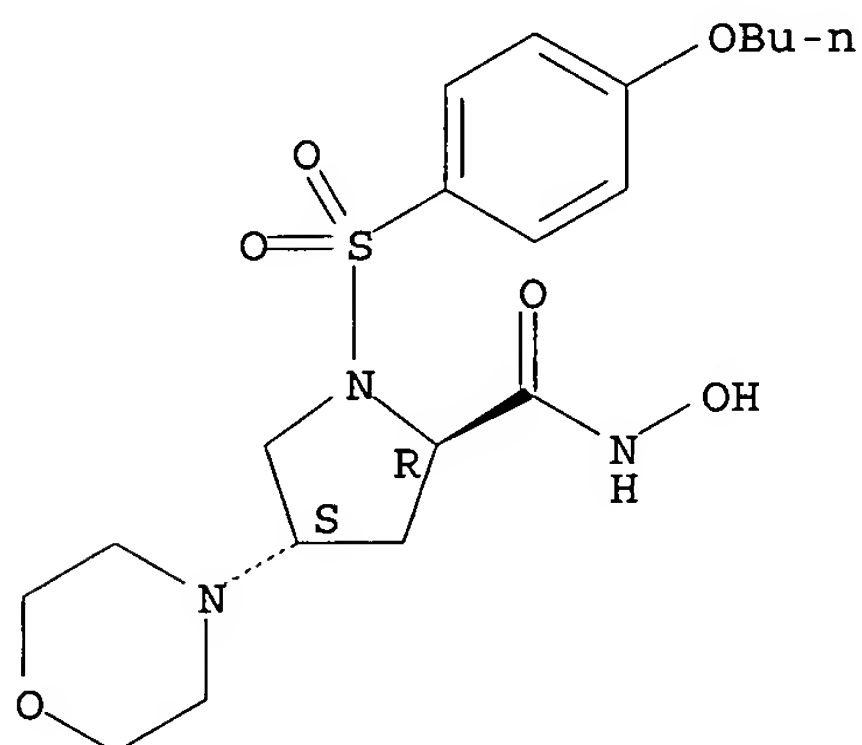
Absolute stereochemistry.



RN 204072-02-6 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(4-morpholinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

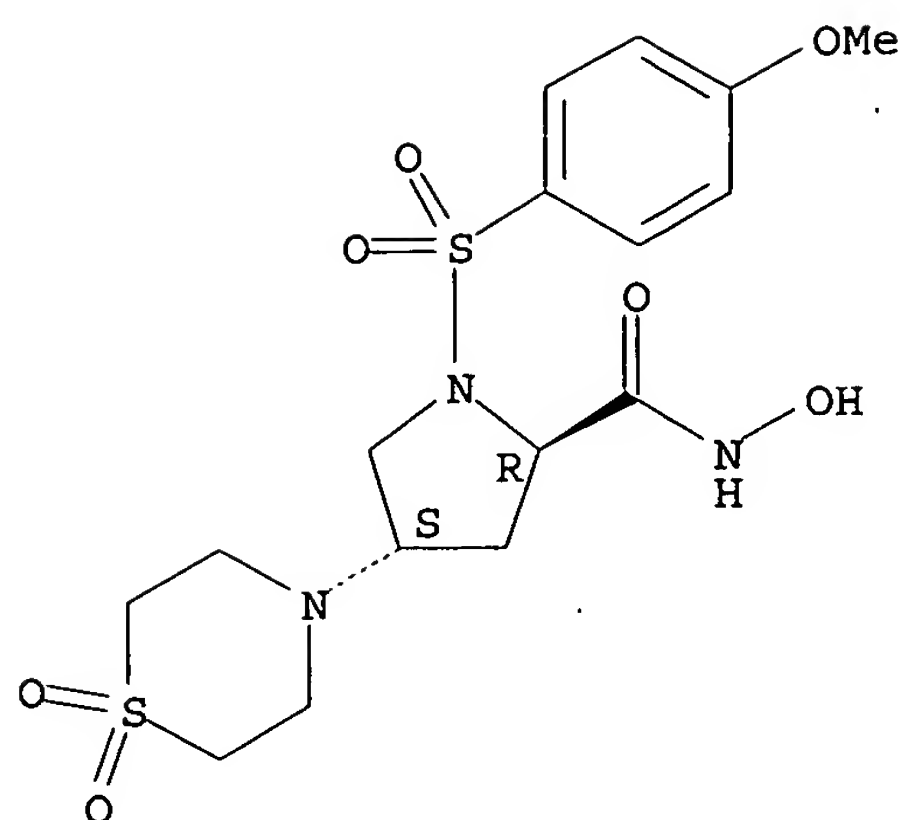
Absolute stereochemistry.



RN 204072-03-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 4-(1,1-dioxido-4-thiomorpholinyl)-N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

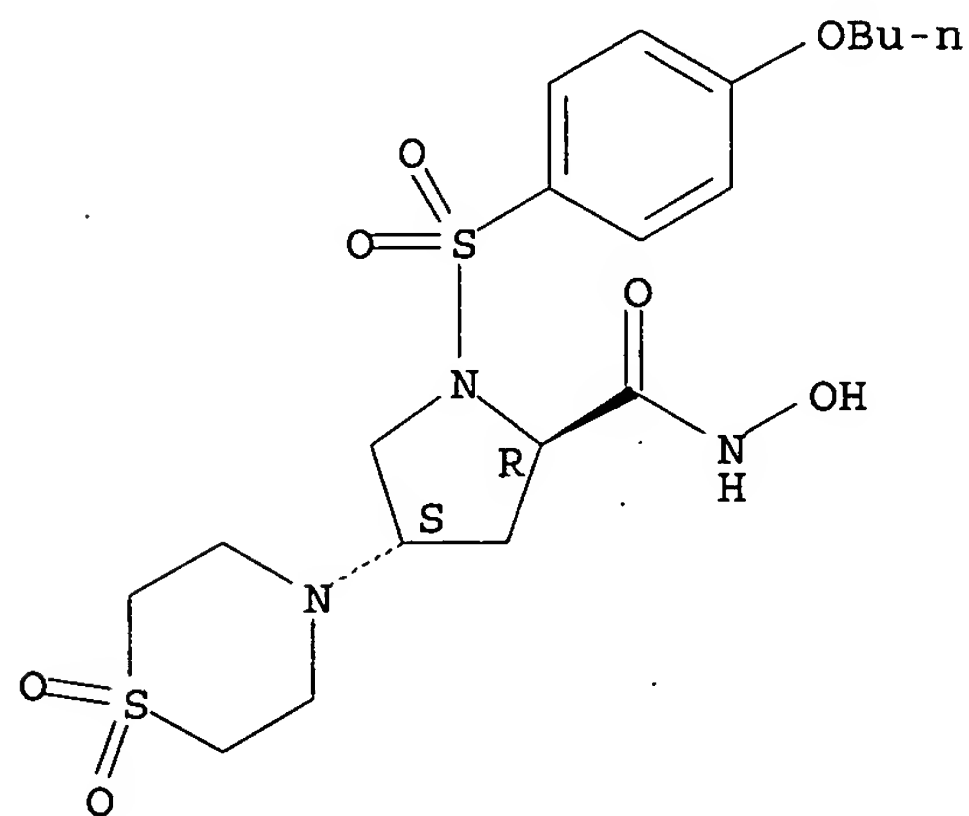
Absolute stereochemistry.



RN 204072-04-8 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-(1,1-dioxido-4-thiomorpholinyl)-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

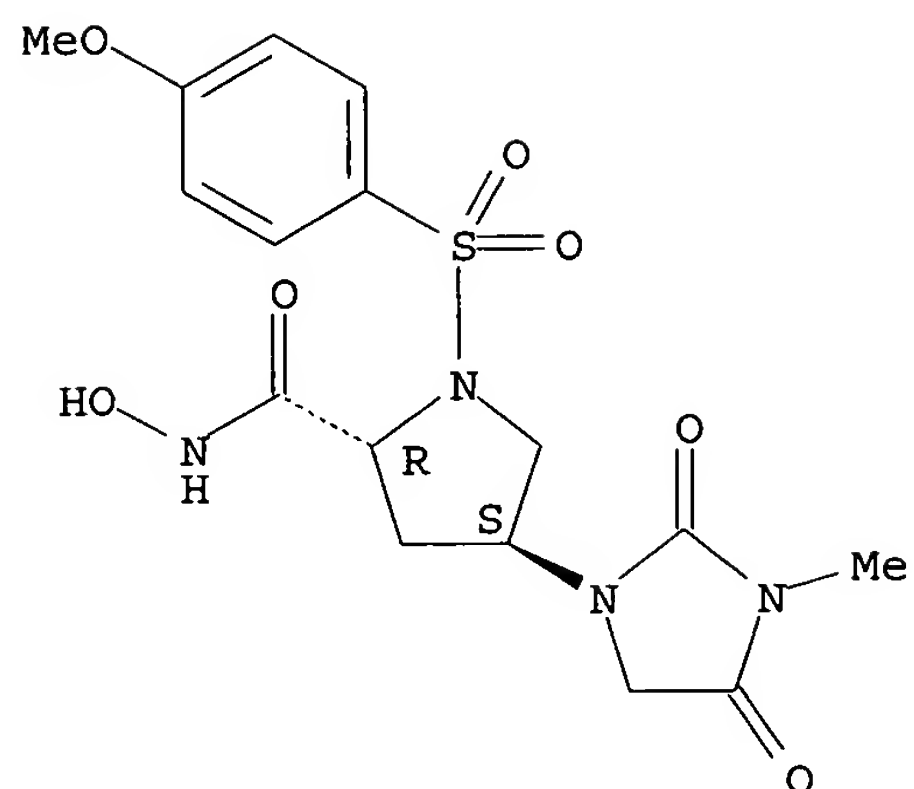
Absolute stereochemistry.



RN 537704-65-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

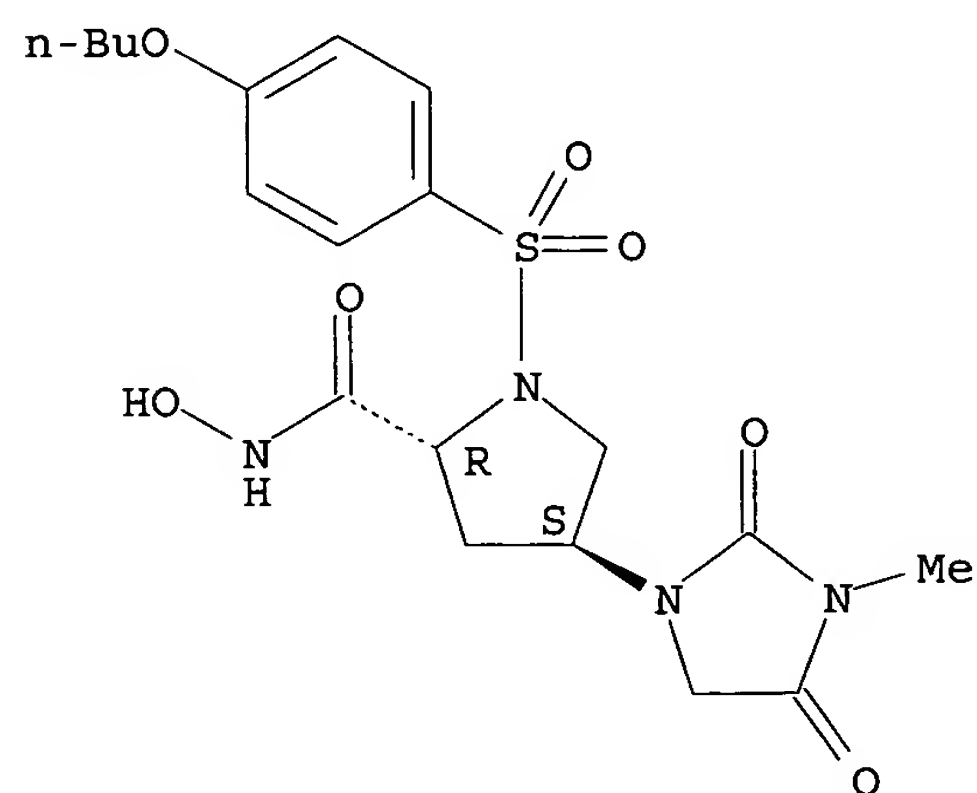
Absolute stereochemistry.



RN 537704-67-9 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

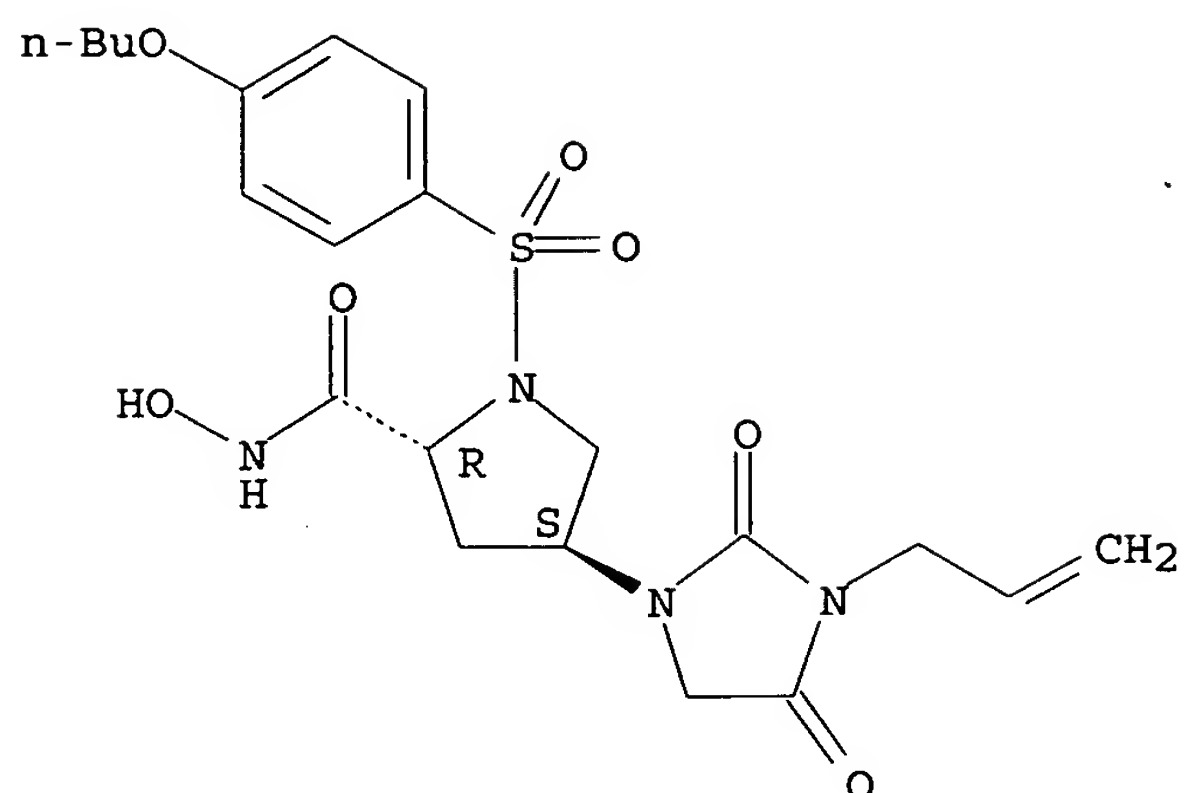
Absolute stereochemistry.



RN 537704-69-1 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-[2,4-dioxo-3-(2-propenyl)-1-imidazolidinyl]-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

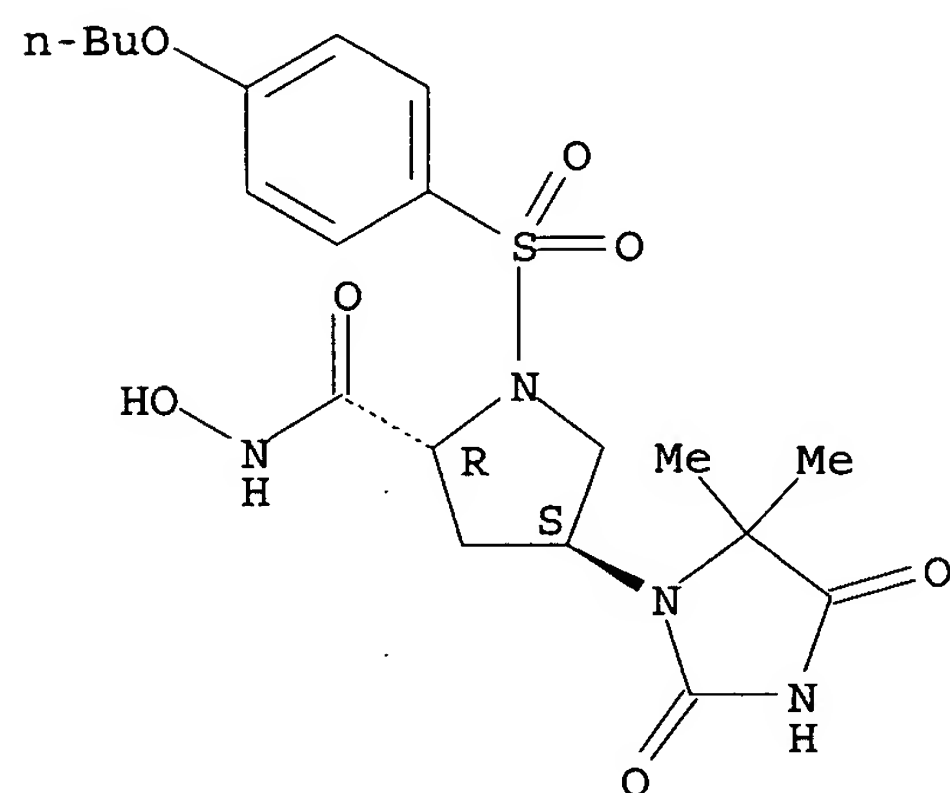
Absolute stereochemistry.



RN 537704-73-7 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-4-(5,5-dimethyl-2,4-dioxo-1-imidazolidinyl)-N-hydroxy-, (2R,4S)- (9CI) (CA INDEX NAME)

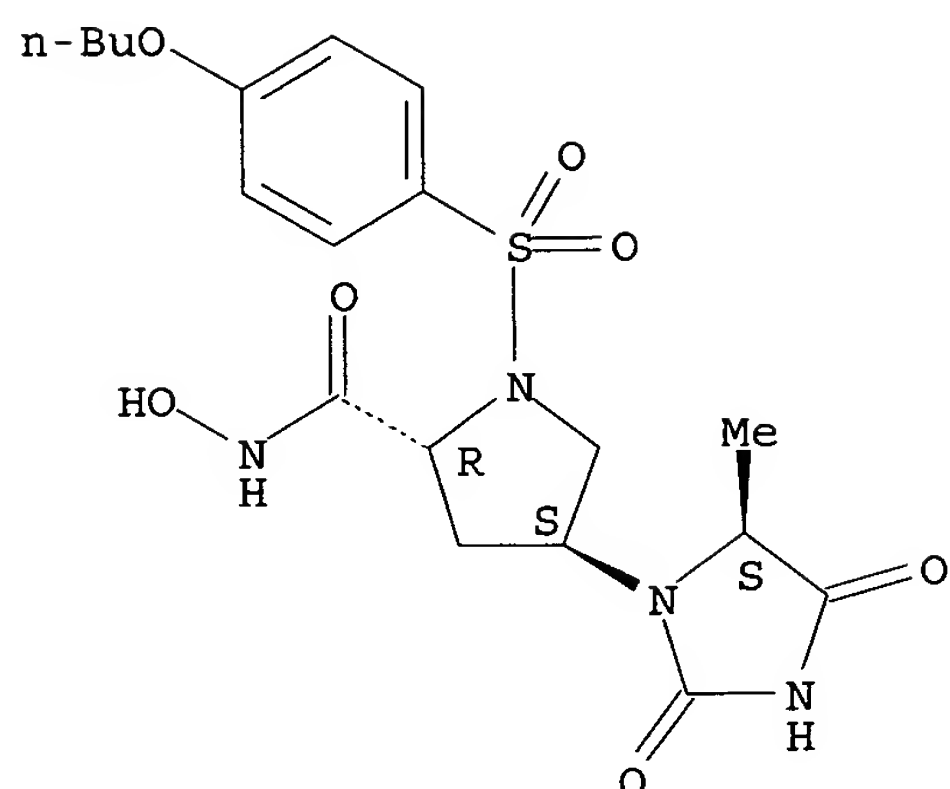
Absolute stereochemistry.



RN 537704-75-9 HCAPLUS

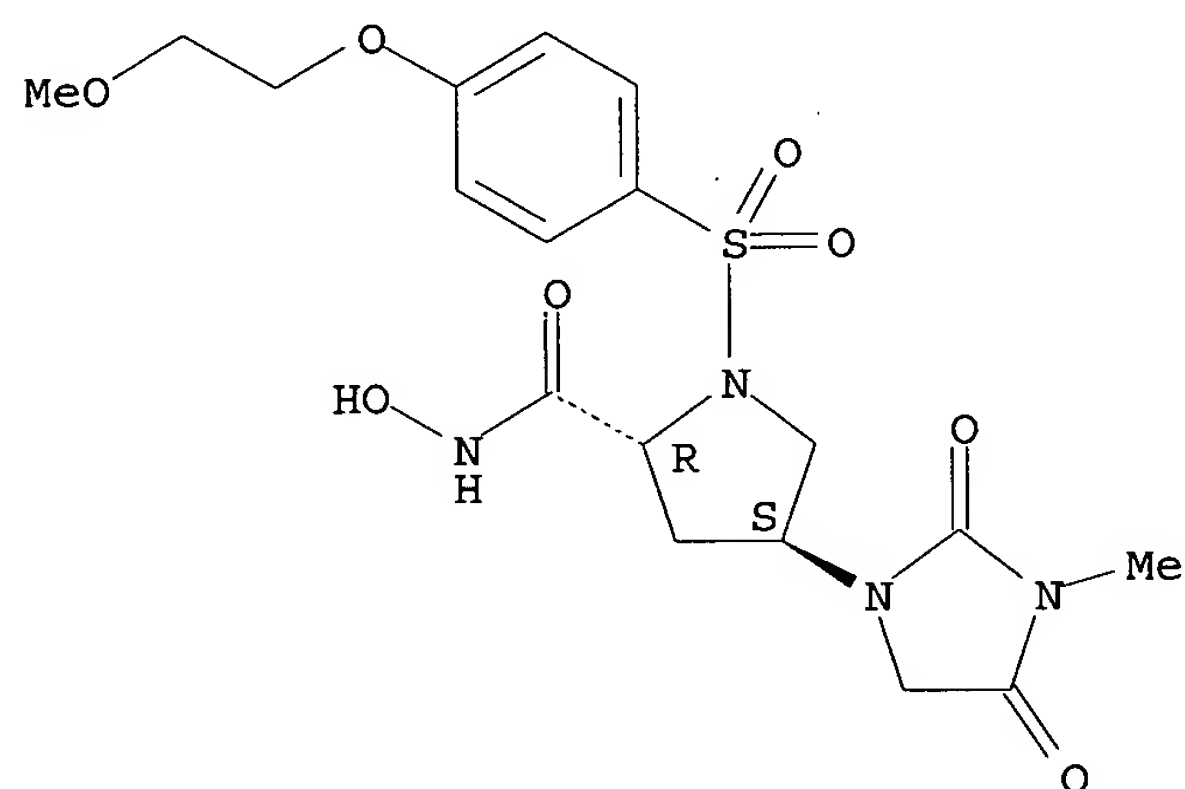
CN 2-Pyrrolidinecarboxamide, 1-[(4-butoxyphenyl)sulfonyl]-N-hydroxy-4-[(5S)-5-methyl-2,4-dioxo-1-imidazolidinyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 537704-77-1 HCAPLUS  
 CN 2-Pyrrolidinecarboxamide, N-hydroxy-1-[[4-(2-methoxyethoxy)phenyl]sulfonyl]-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-, (2R,4S)- (9CI) (CA INDEX NAME)

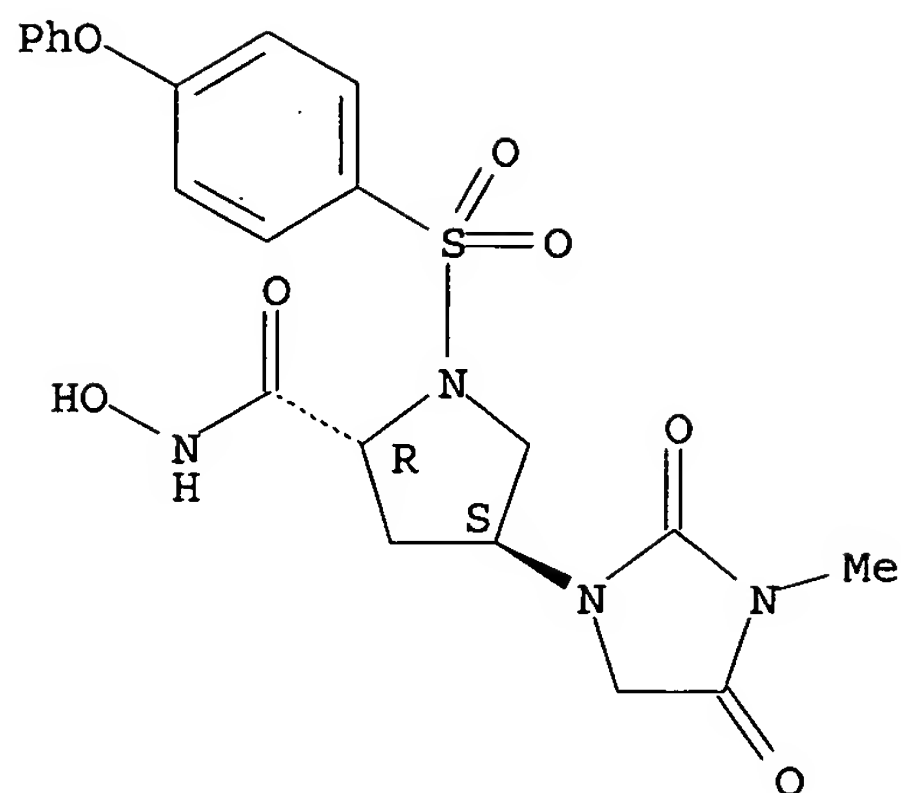
Absolute stereochemistry.



RN 537704-79-3 HCAPLUS  
 CN 2-Pyrrolidinecarboxamide, N-hydroxy-4-(3-methyl-2,4-dioxo-1-imidazolidinyl)-1-[(4-phenoxyphenyl)sulfonyl]-, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

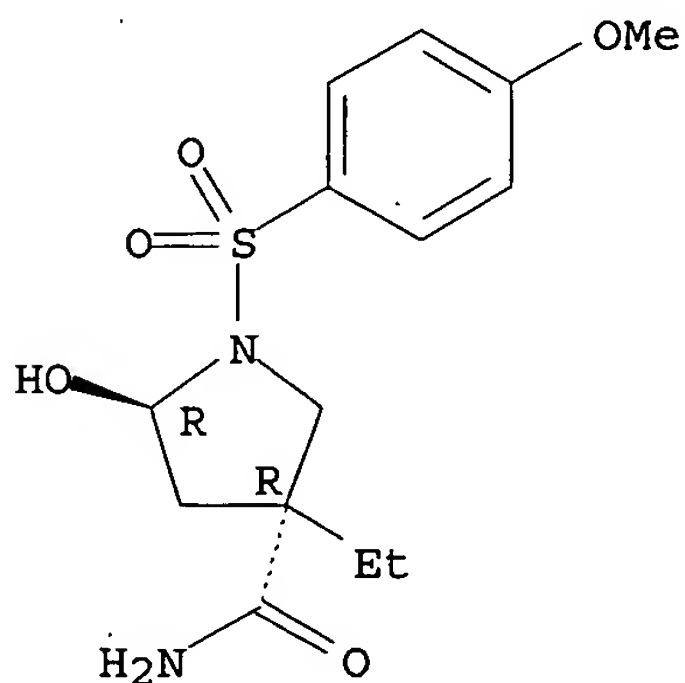




RN 537704-80-6 HCAPLUS

CN 3-Pyrrolidinecarboxamide, 3-ethyl-5-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, (3R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L32 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:22851 HCAPLUS

DOCUMENT NUMBER: 138:55878

TITLE: Preparation of bispiperidines as antibacterial agents and inhibitors of phosphopantetheine adenylyl transferase.

INVENTOR(S): Lampe, Thomas; Ehlert, Kerstin; Freiberg, Christoph; Schiffer, Guido

PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

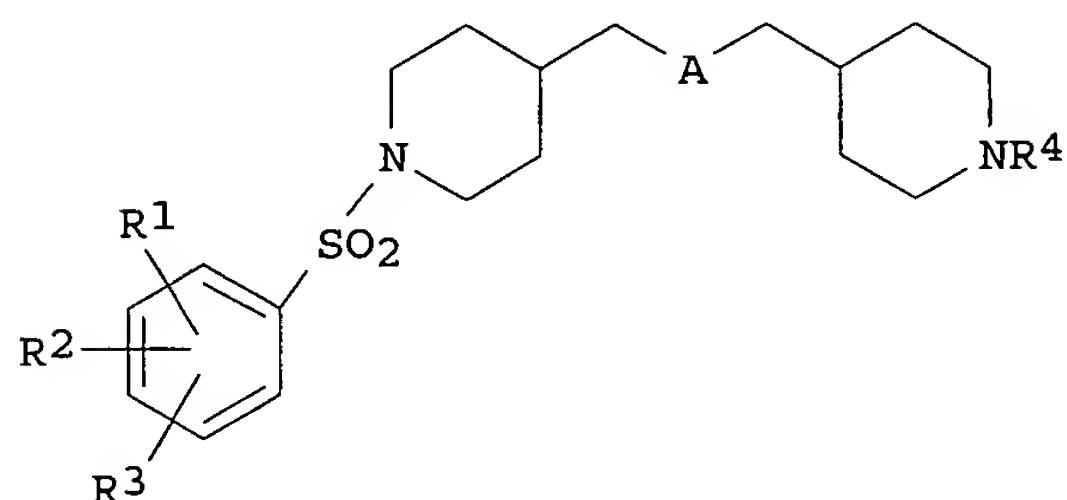
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002534	A1	20030109	WO 2002-EP6640	20020617 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10138234 A1 20030109 DE 2001-10138234 20010803 <--  
 PRIORITY APPLN. INFO.: DE 2001-10131134 A 20010628  
 DE 2001-10138234 A 20010803

OTHER SOURCE(S): MARPAT 138:55878  
 GI



AB Use of title compds. [I; A = O, (CH<sub>2</sub>)<sub>n</sub>; n = 0-2; R<sub>1</sub>-R<sub>3</sub> = H, halo, alkyl, cycloalkyl, alkoxy, alkoxy carbonyl, etc.; or R<sub>1</sub>R<sub>2</sub> = C<sub>6</sub> aryl, 5-8 membered heterocyclyl; R<sub>3</sub> = H, halo, alkyl, cycloalkyl, alkoxy, alkoxy carbonyl, alkyl carbonyl, amino, etc.; R<sub>4</sub> = H, alkyl, cycloalkyl, alkyl carbonyl, cycloalkyl carbonyl, aryl carbonyl, etc.], for treatment of bacterial infection is claimed. I are useful for the treatment of diseases caused by bacteria requiring phosphopantetheine adenylyl transferase (CoaD) enzyme for CoA synthesis. Tested I (general preparation given) inhibited CoaD activity with IC<sub>50</sub> = 0.65-12.5 μM, and showed min. inhibitory concns. of <0.2 μM to 100 μM against B. subtilis Al 796.

IT 219140-19-9P 341020-80-2P 479618-65-0P  
 479618-66-1P 479618-67-2P 479618-68-3P  
 479618-69-4P 479618-70-7P 479618-71-8P  
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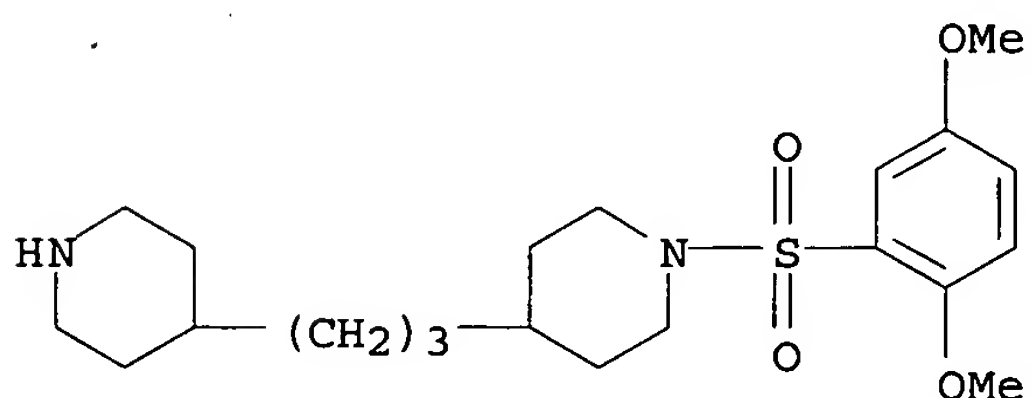
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of bispiperidines as antibacterial agents and  
 inhibitors of phosphopantetheine adenylyl transferase)

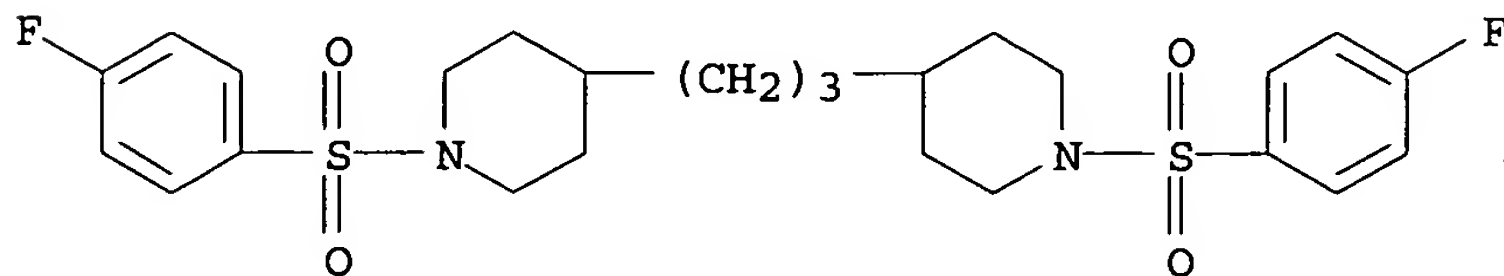
RN 219140-19-9 HCAPLUS

CN Piperidine, 1-[(2,5-dimethoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-  
 (9CI) (CA INDEX NAME)



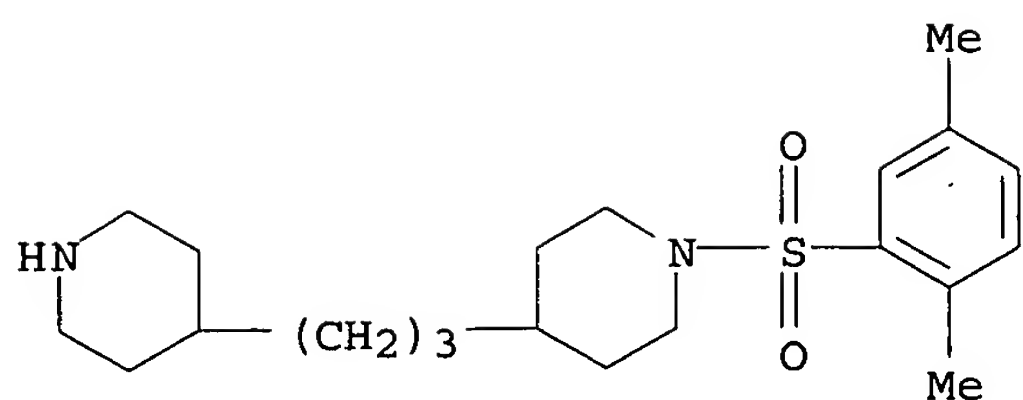
RN 341020-80-2 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-fluorophenyl)sulfonyl]]- (9CI)  
 (CA INDEX NAME)



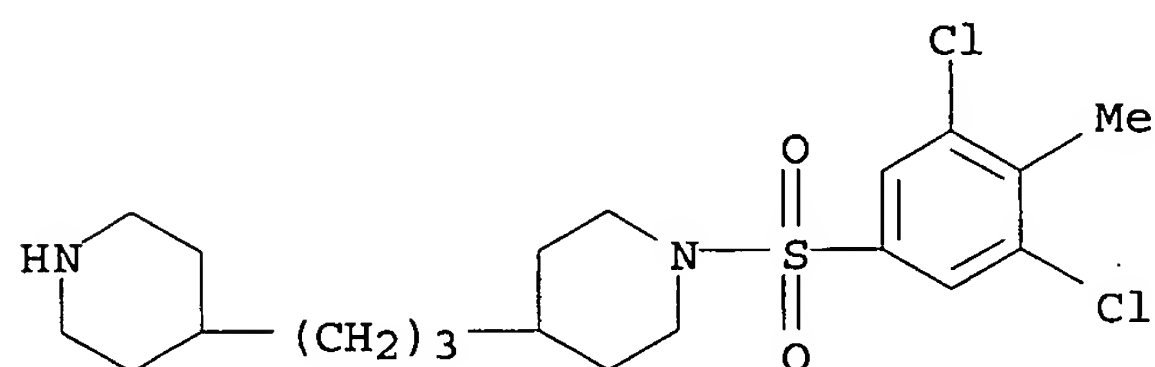
RN 479618-65-0 HCAPLUS

CN Piperidine, 1-[(2,5-dimethylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-  
 (9CI) (CA INDEX NAME)



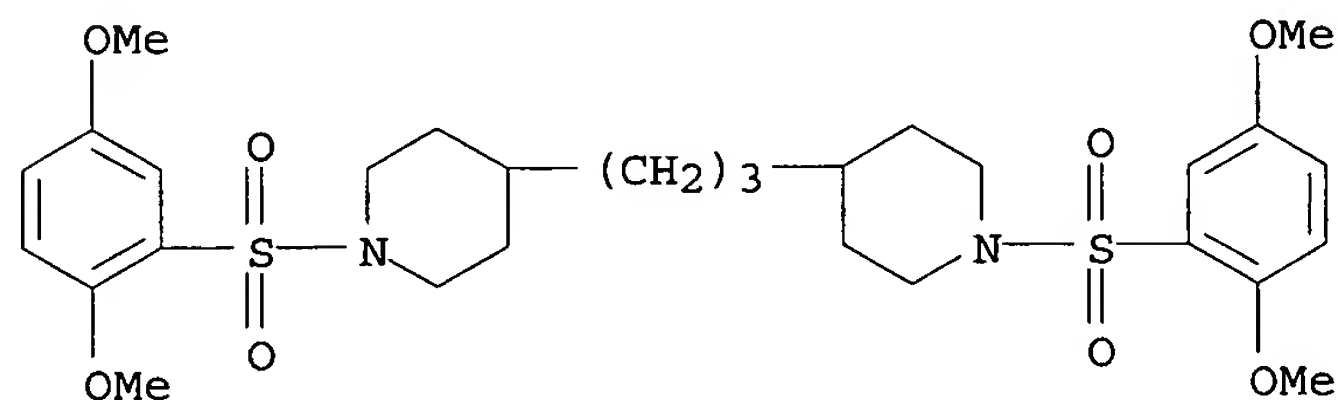
RN 479618-66-1 HCAPLUS

CN Piperidine, 1-[(3,5-dichloro-4-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



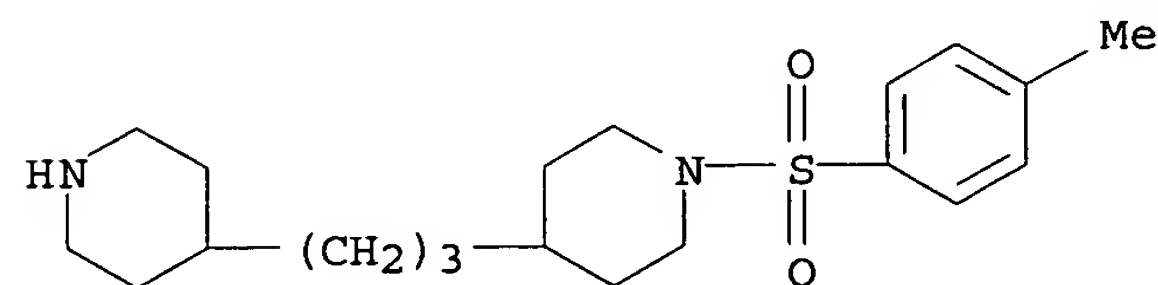
RN 479618-67-2 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



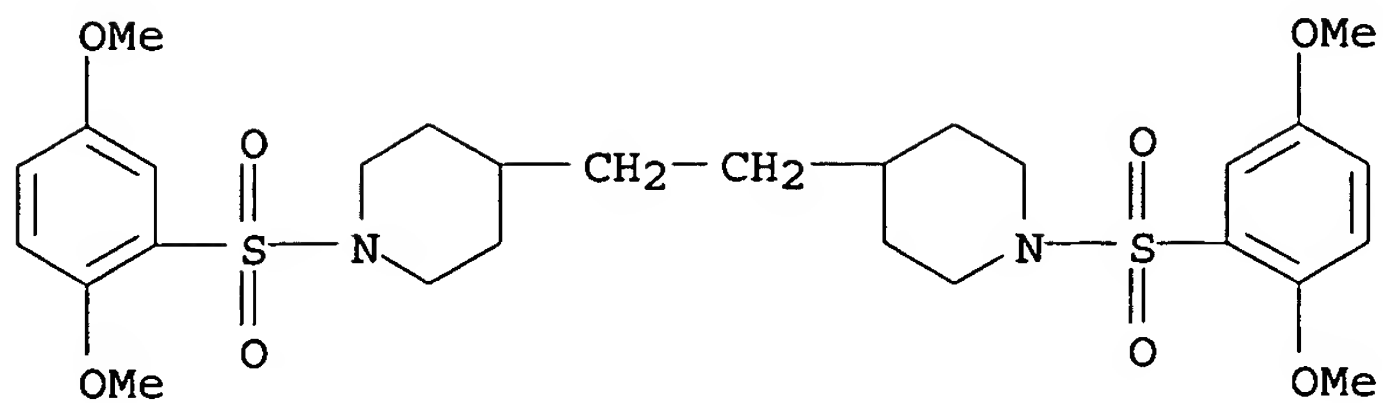
RN 479618-68-3 HCAPLUS

CN Piperidine, 1-[(4-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

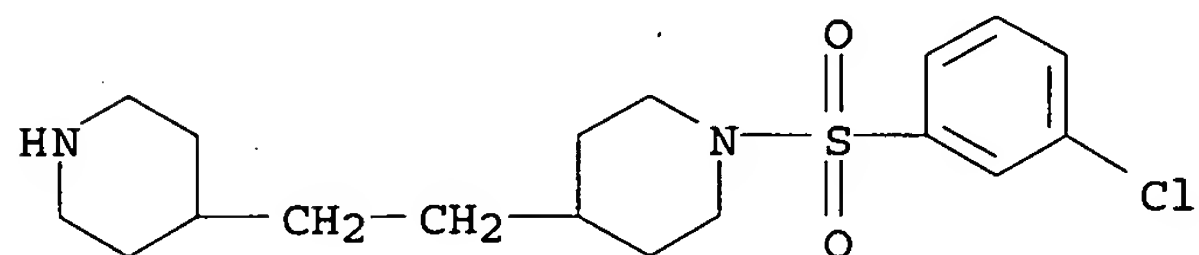


RN 479618-69-4 HCAPLUS

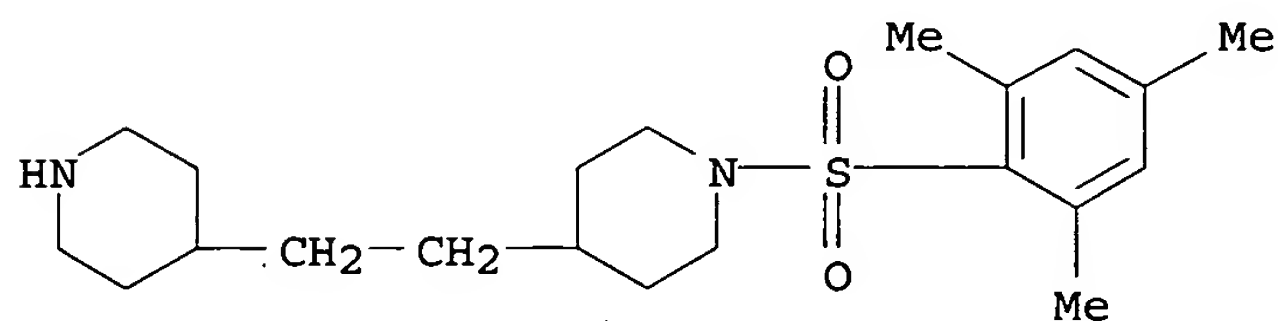
CN Piperidine, 4,4'-(1,2-ethanediyl)bis[1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



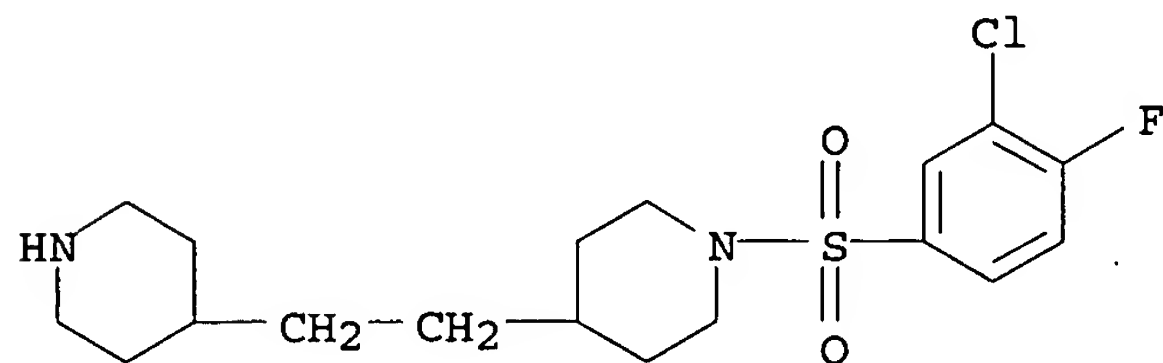
RN 479618-70-7 HCAPLUS  
 CN Piperidine, 1-[(3-chlorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI)  
 (CA INDEX NAME)



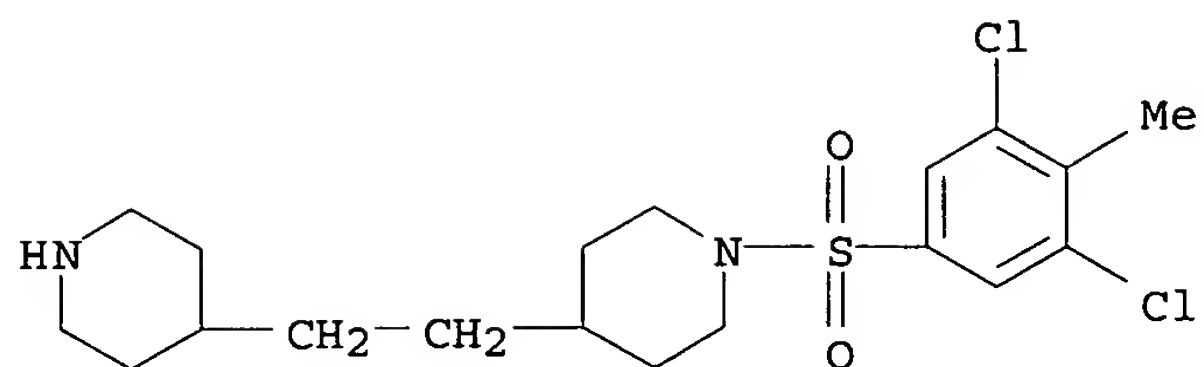
RN 479618-71-8 HCAPLUS  
 CN Piperidine, 4-[2-(4-piperidinyl)ethyl]-1-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 479618-72-9 HCAPLUS  
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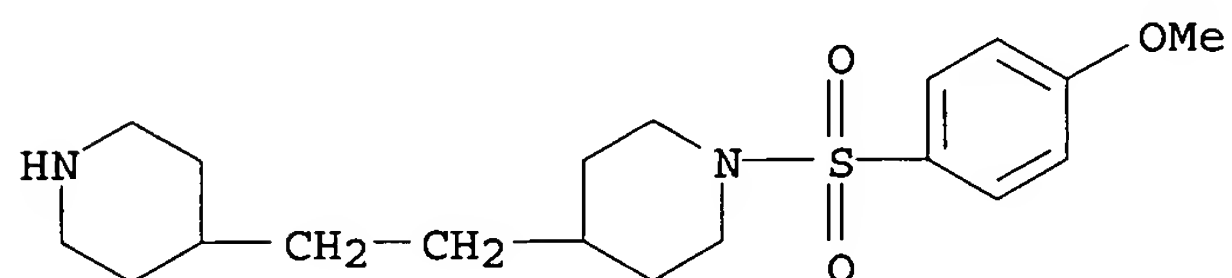


RN 479618-73-0 HCAPLUS  
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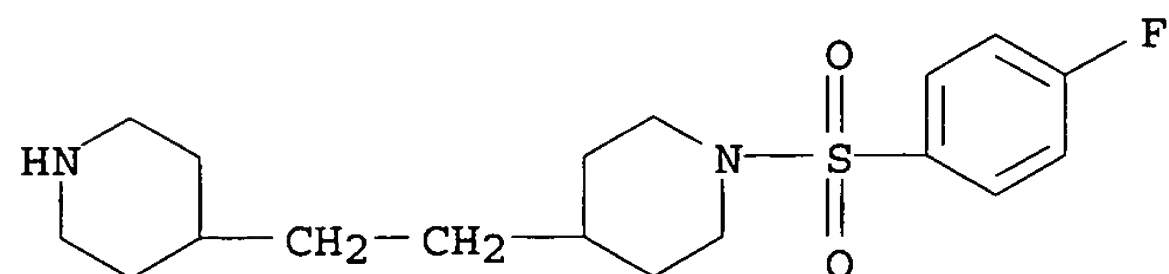
RN 479618-74-1 HCAPLUS

CN Piperidine, 1-[(4-methoxyphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



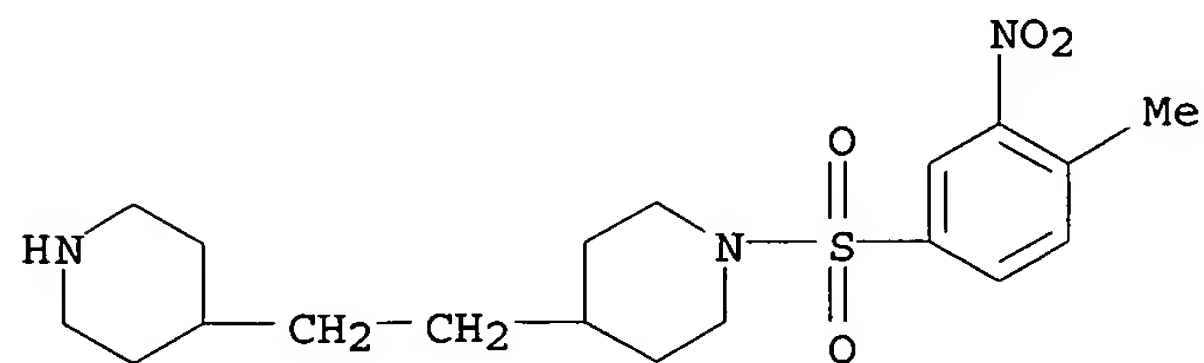
RN 479618-75-2 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



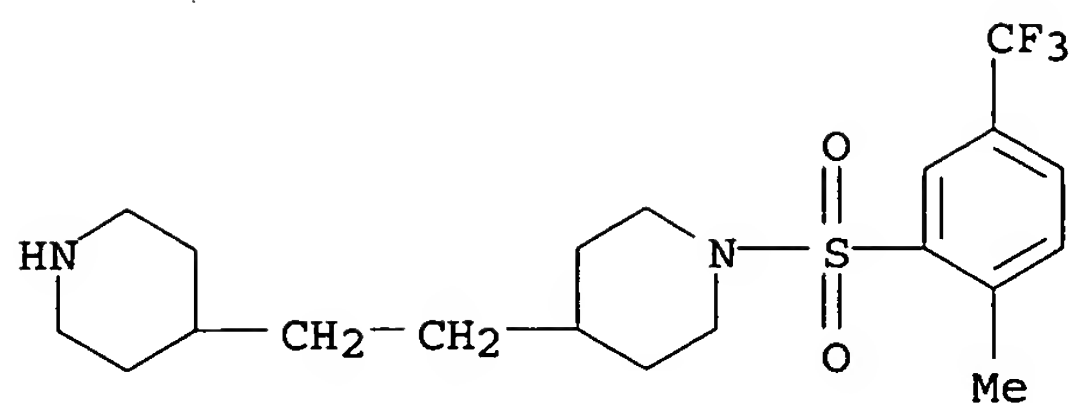
RN 479618-76-3 HCAPLUS

CN Piperidine, 1-[(4-methyl-3-nitrophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



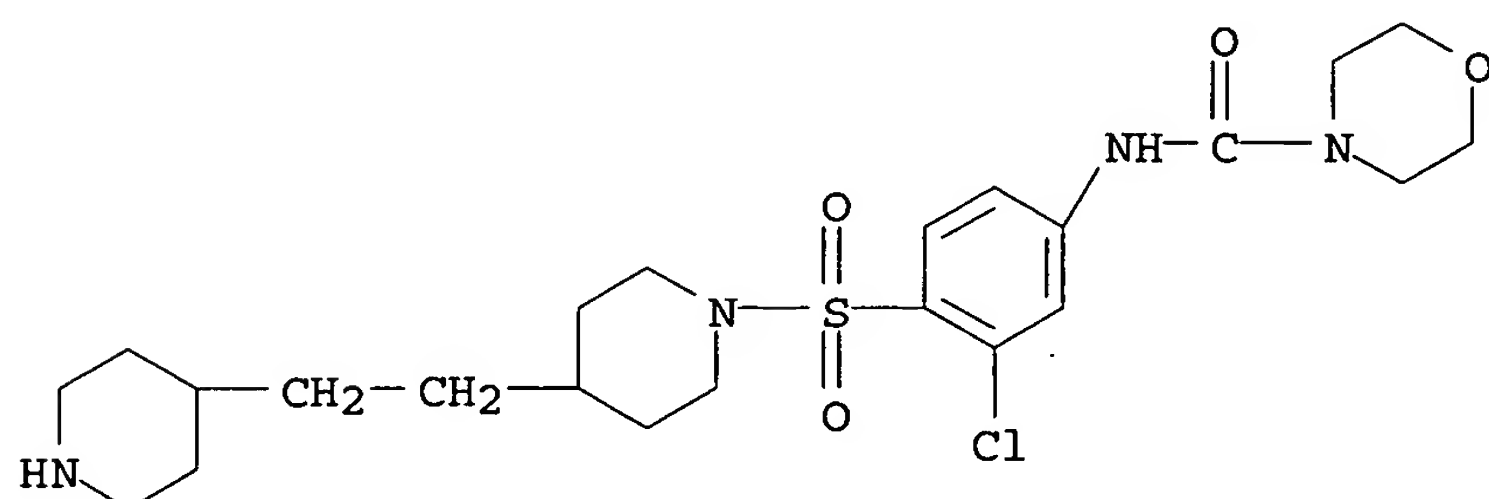
RN 479618-77-4 HCAPLUS

CN Piperidine, 1-[[2-methyl-5-(trifluoromethyl)phenyl]sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



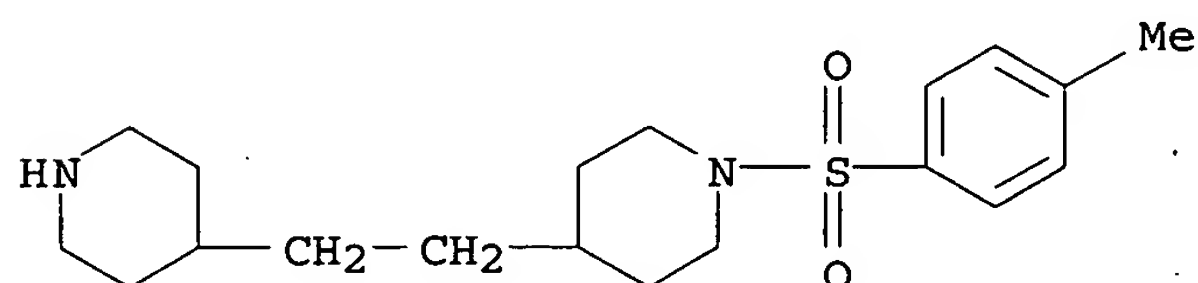
RN 479618-78-5 HCAPLUS

CN 4-Morpholinecarboxamide, N-[3-chloro-4-[[4-[2-(4-piperidinyl)ethyl]-1-piperidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)



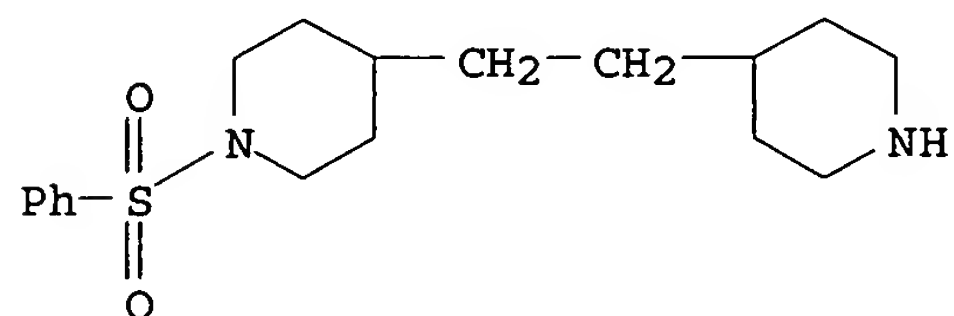
RN 479618-79-6 HCAPLUS

CN Piperidine, 1-[(4-methylphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



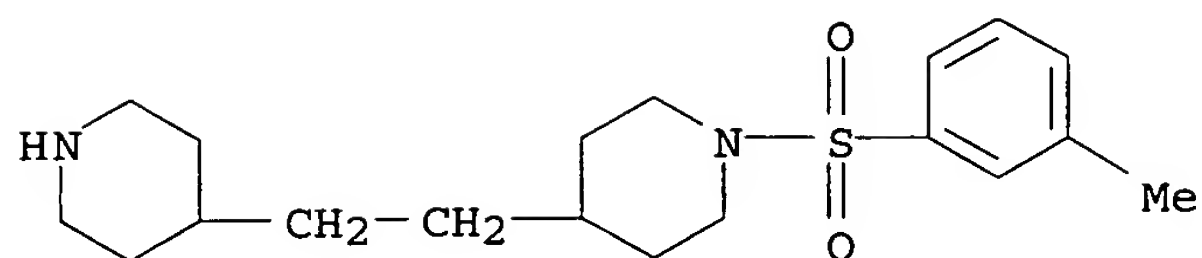
RN 479618-80-9 HCAPLUS

CN Piperidine, 1-(phenylsulfonyl)-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



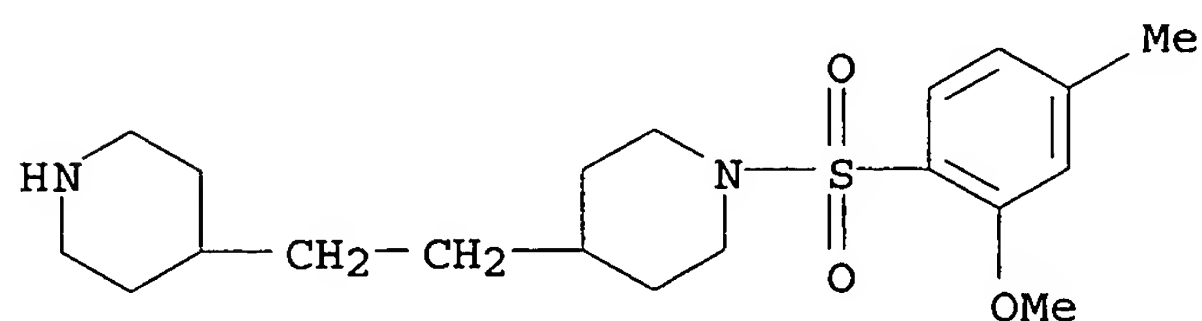
RN 479618-81-0 HCAPLUS

CN Piperidine, 1-[(3-methylphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



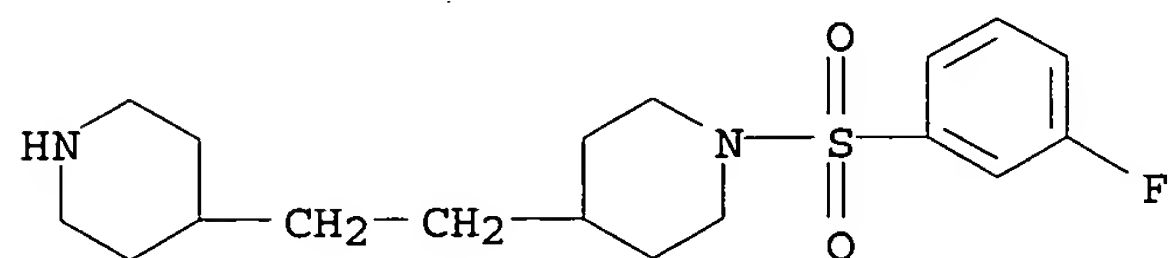
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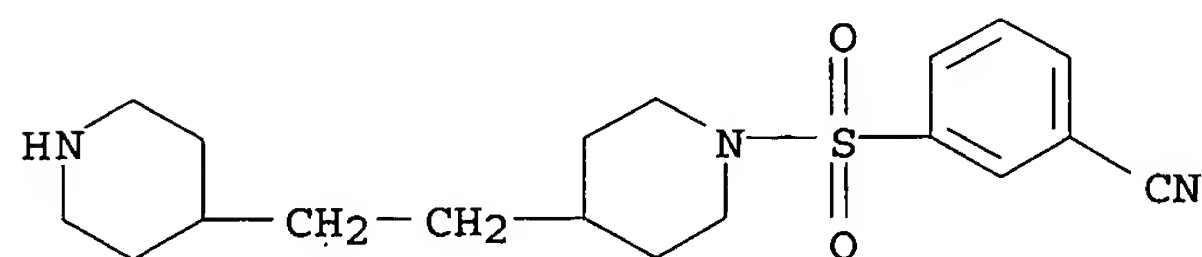
RN 479618-83-2 HCAPLUS

CN Piperidine, 1-[(3-fluorophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



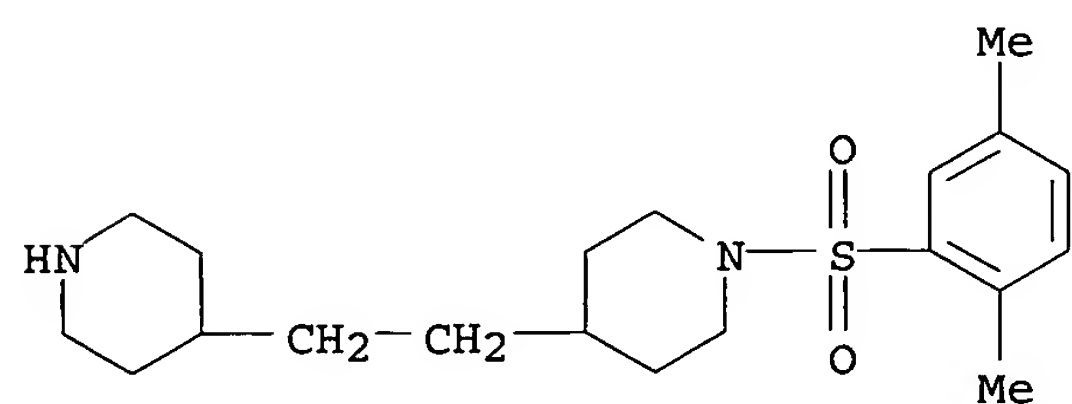
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CN Piperidine, 1-[(3-cyanophenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



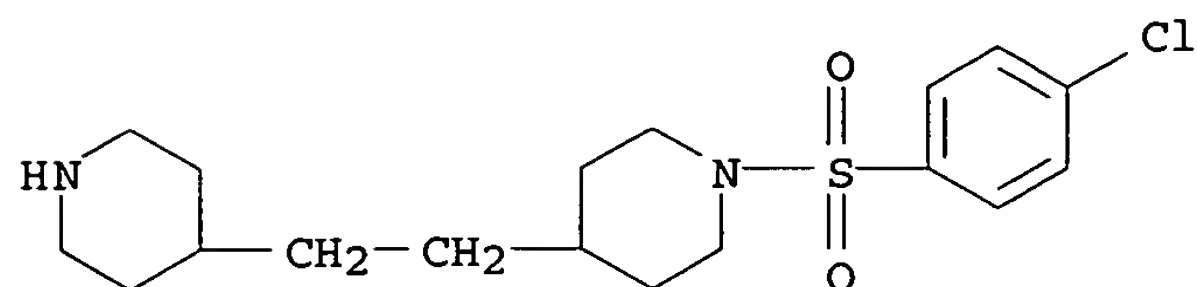
RN 479618-85-4 HCAPLUS

CN Piperidine, 1-[(2,5-dimethylphenyl)sulfonyl]-4-[2-(4-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

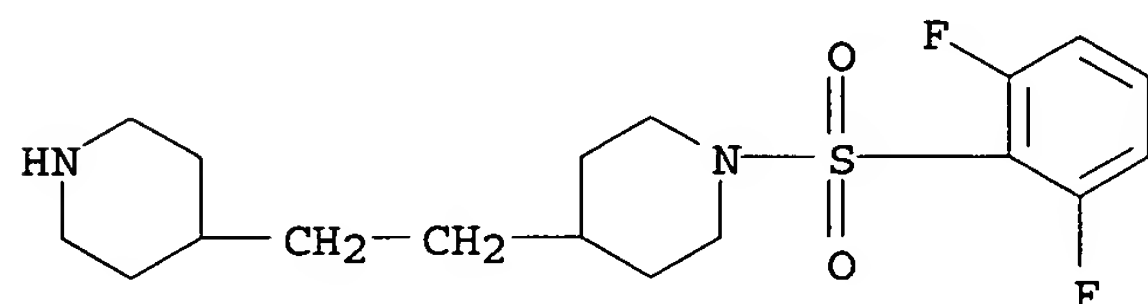




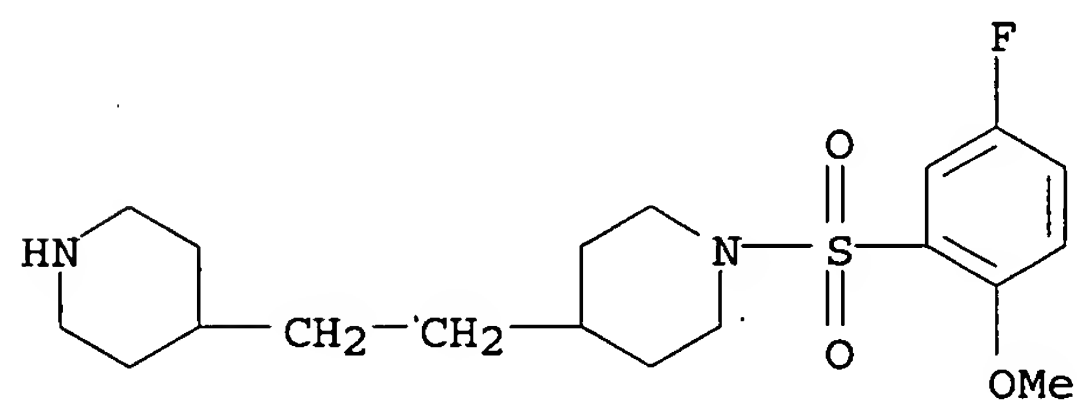
RN 479618-86-5 HCAPLUS  
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 (CA INDEX NAME)



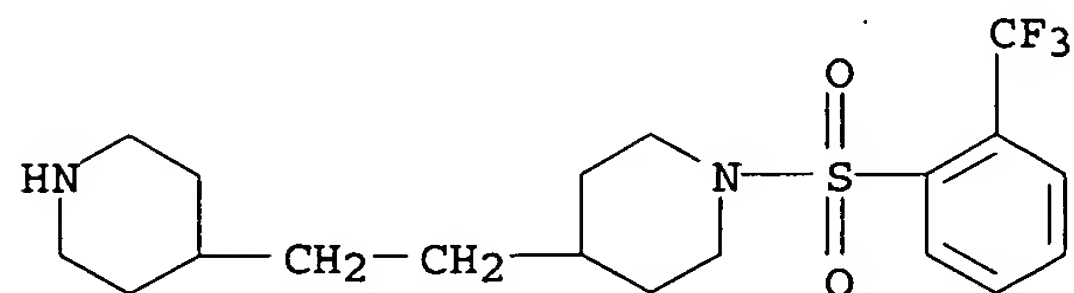
RN 479618-87-6 HCAPLUS  
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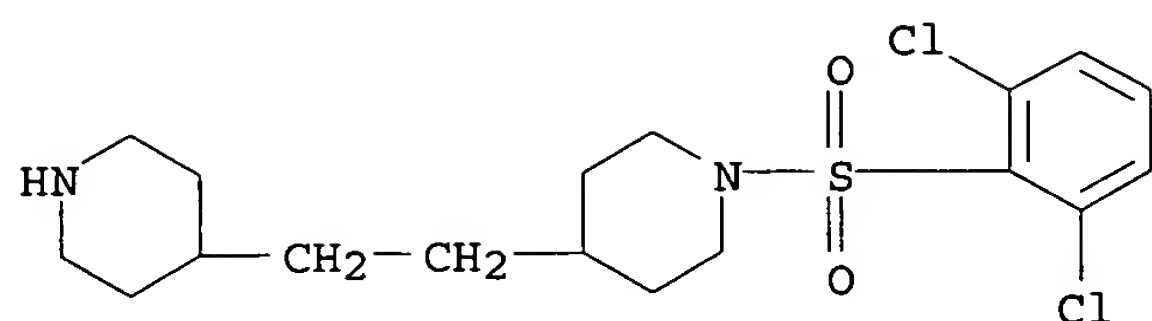
RN 479618-88-7 HCAPLUS  
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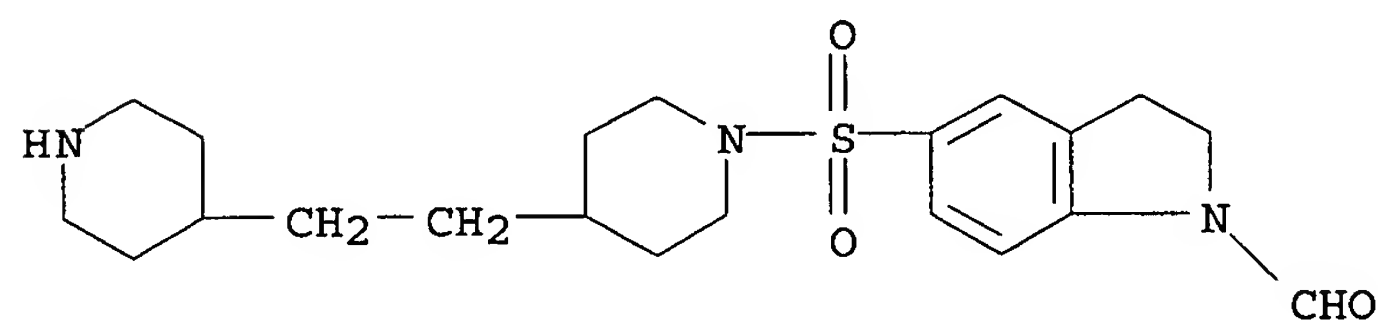
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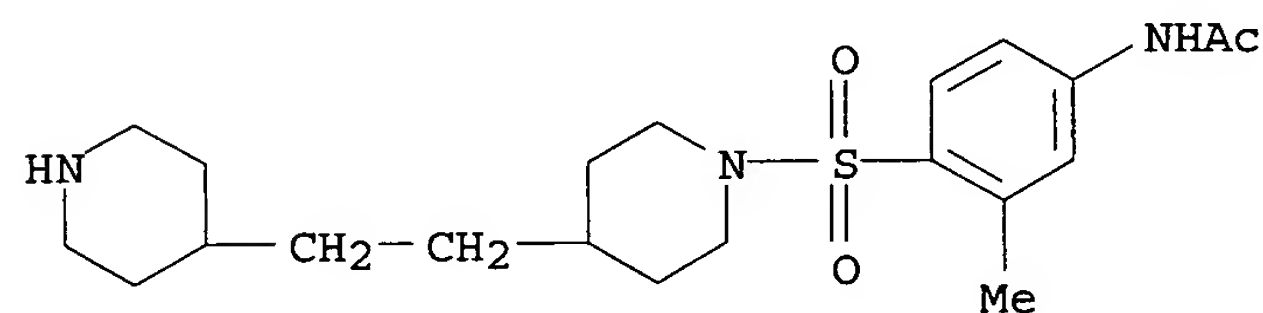
RN 479618-90-1 HCAPLUS  
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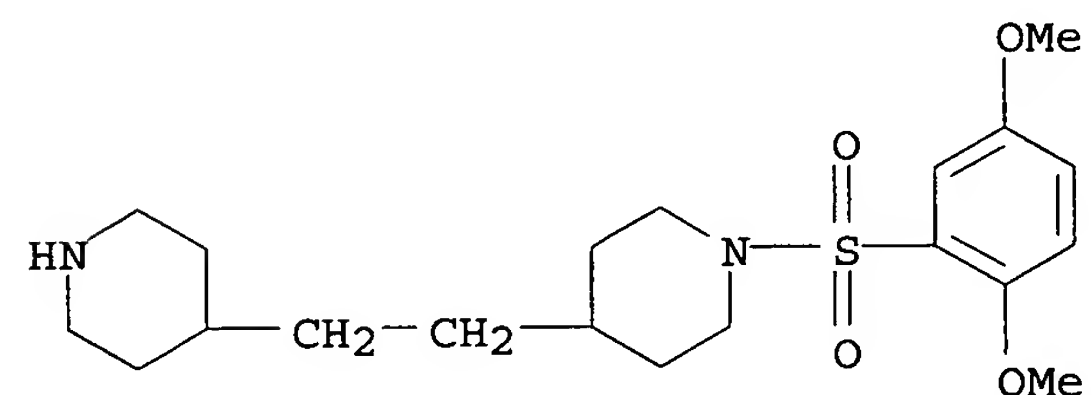
RN 479618-91-2 HCAPLUS  
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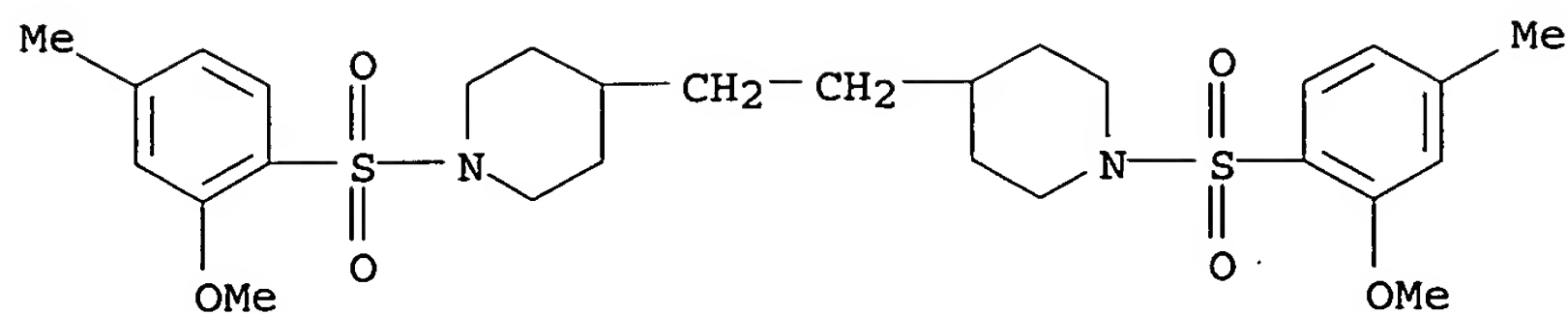
RN 479618-92-3 HCAPLUS  
 CN Acetamide, N-[3-methyl-4-[[4-[2-(4-piperidinyl)ethyl]-1-piperidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)



RN 479618-93-4 HCAPLUS  
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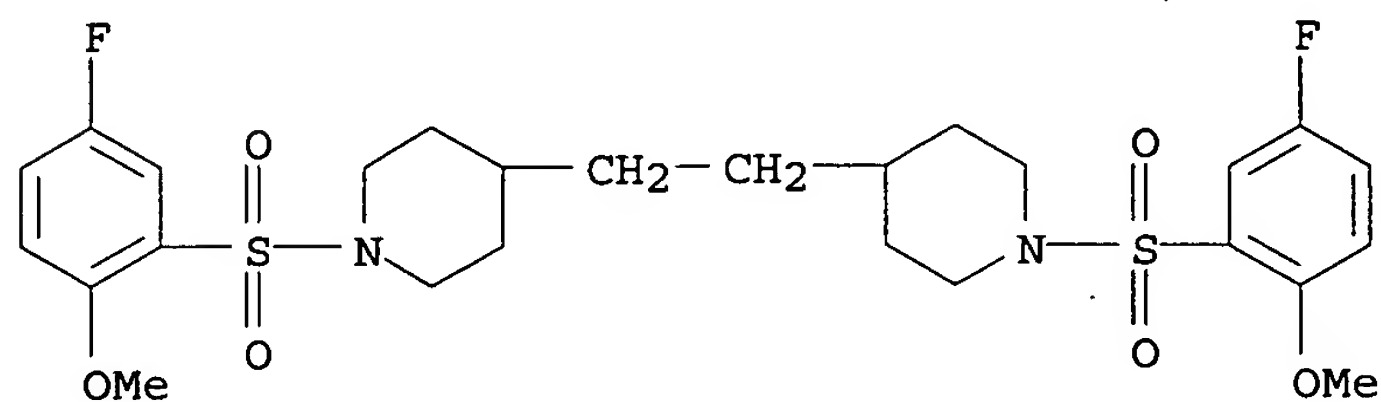


RN 479618-94-5 HCAPLUS  
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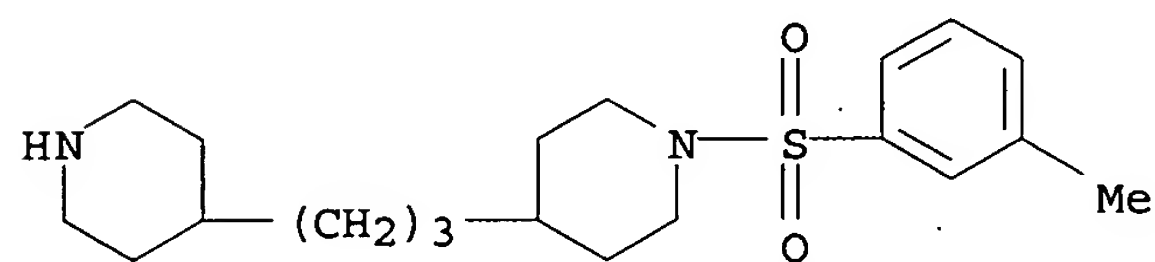
RN 479618-95-6 HCAPLUS

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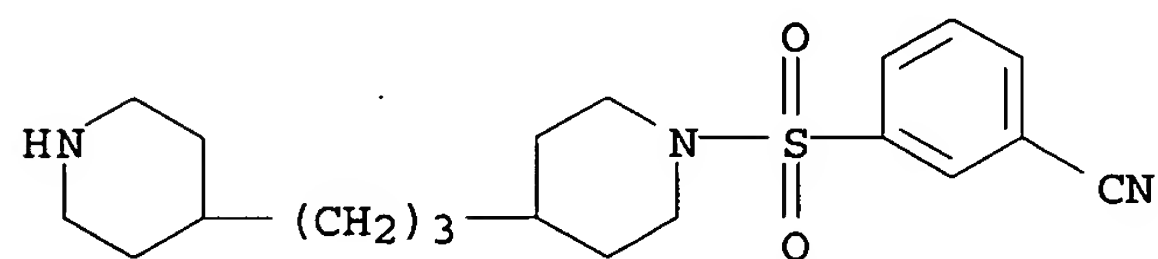
RN 479618-96-7 HCAPLUS

CN Piperidine, 1-[(3-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl] - (9CI) (CA INDEX NAME)



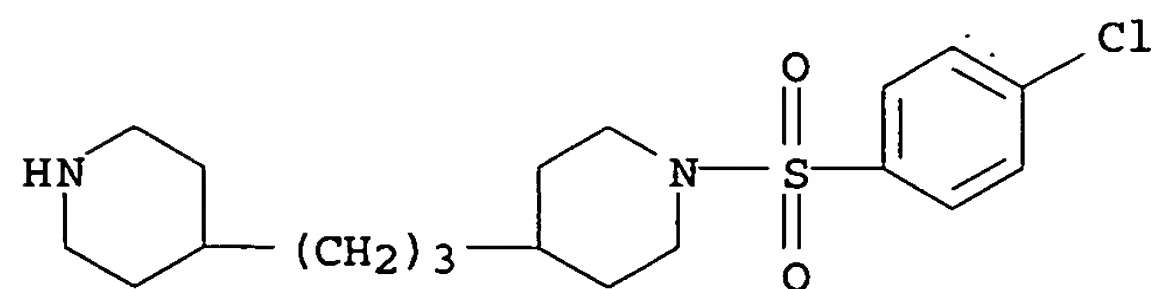
RN 479618-97-8 HCAPLUS

CN Piperidine, 1-[(3-cyanophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl] - (9CI) (CA INDEX NAME)

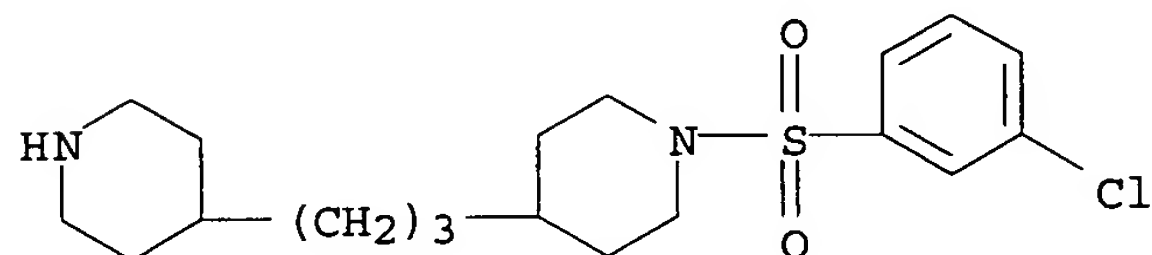


RN 479618-98-9 HCAPLUS

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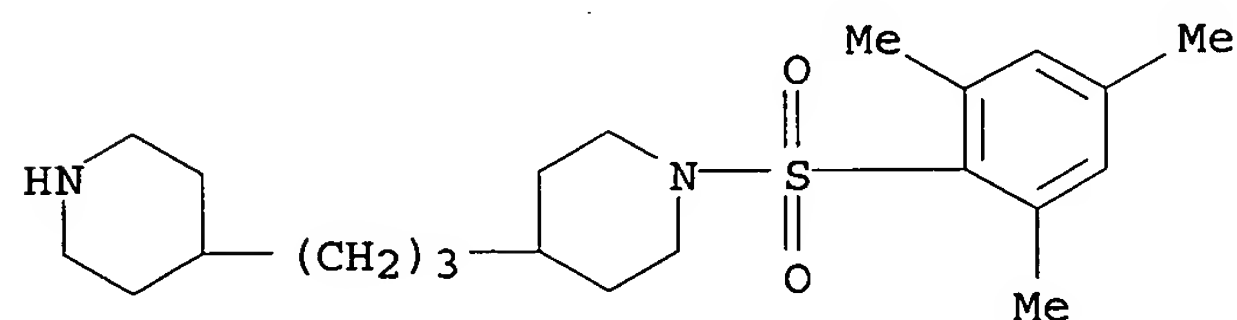


RN 479618-99-0 HCAPLUS

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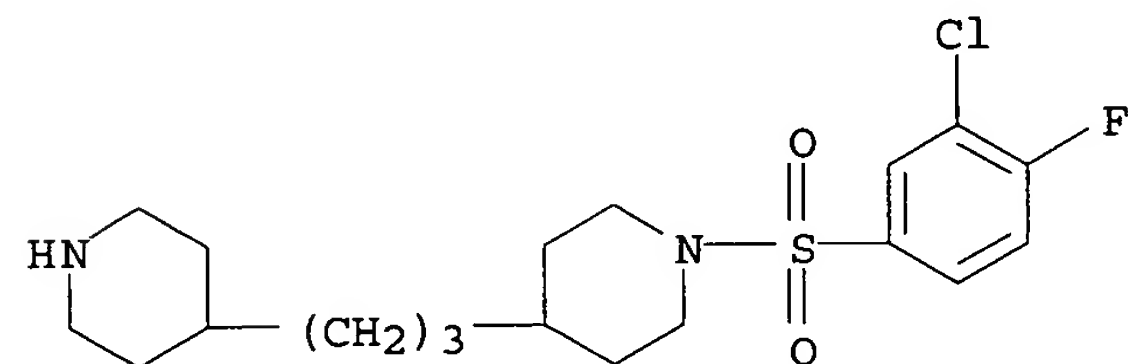
RN 479619-00-6 HCAPLUS

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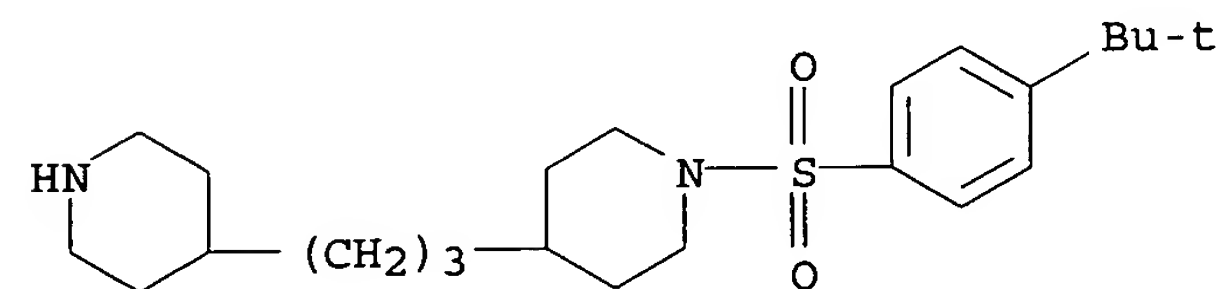
RN 479619-01-7 HCAPLUS

CN Piperidine, 1-[(3-chloro-4-fluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



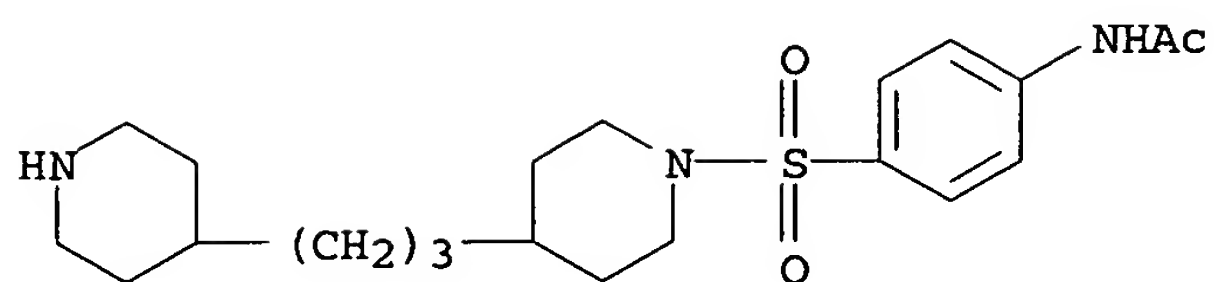
RN 479619-02-8 HCAPLUS

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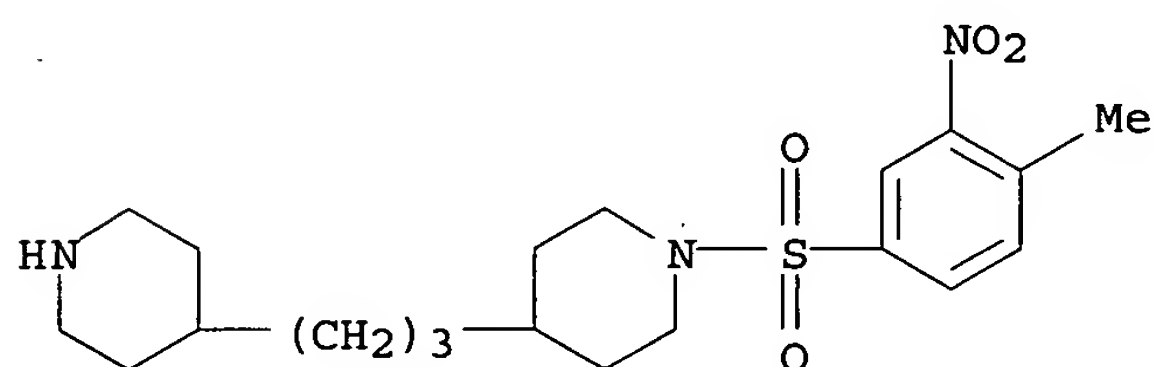
RN 479619-03-9 HCAPLUS

CN Acetamide, N-[4-[[4-[3-(4-piperidinyl)propyl]-1-piperidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)



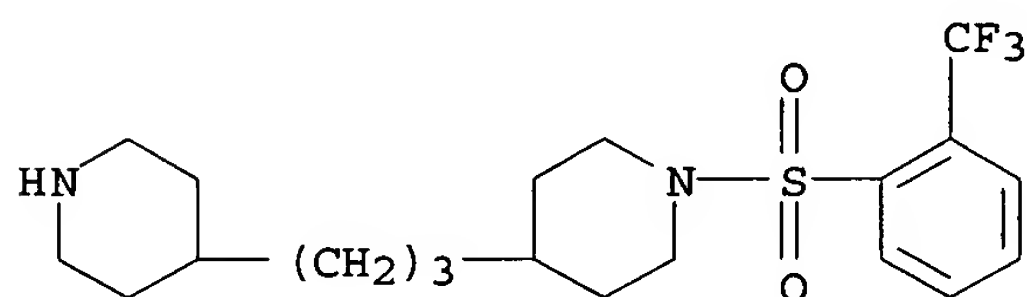
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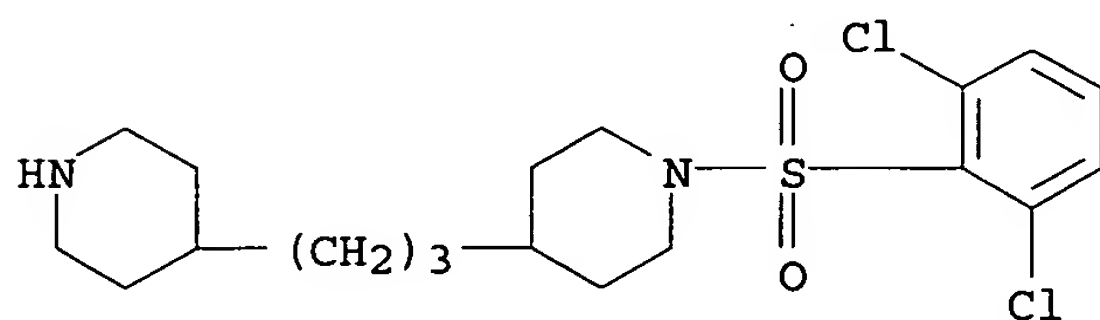
RN 479619-05-1 HCAPLUS

CN Piperidine, 4-[3-(4-piperidinyl)propyl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



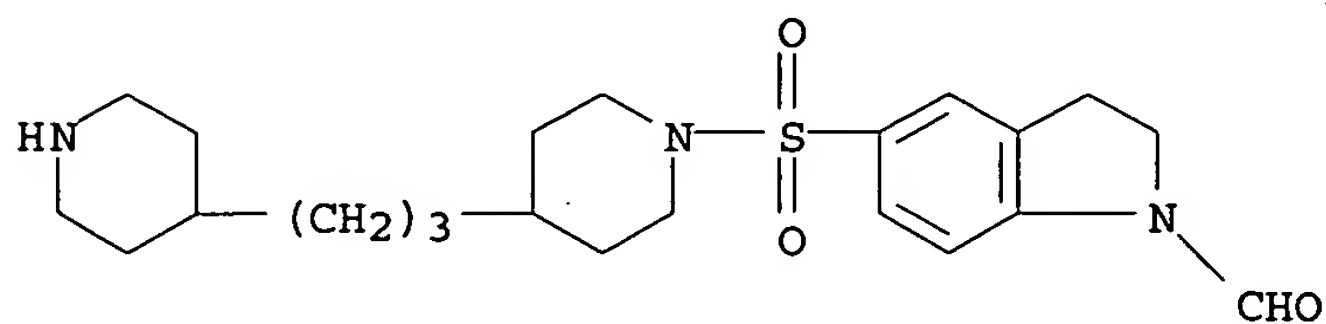
RN 479619-06-2 HCAPLUS

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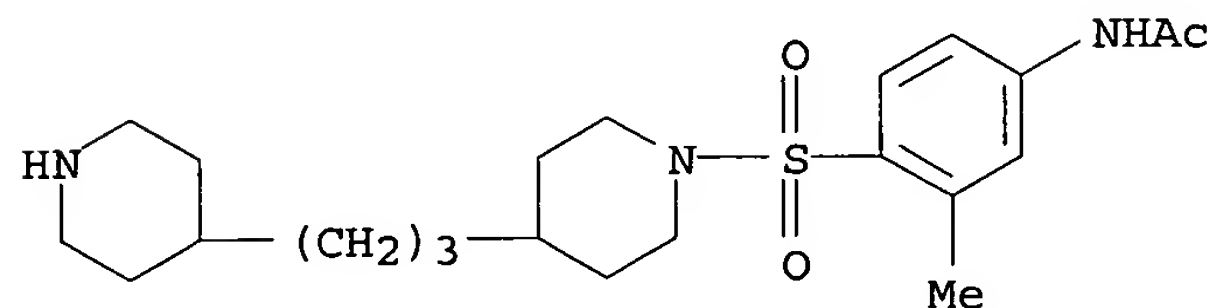
RN 479619-07-3 HCAPLUS

CN Piperidine, 1-[(1-formyl-2,3-dihydro-1H-indol-5-yl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



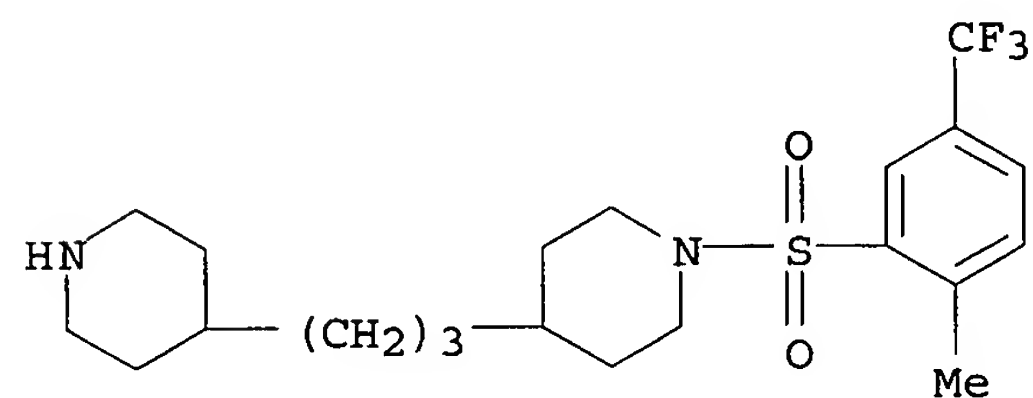
RN 479619-08-4 HCAPLUS

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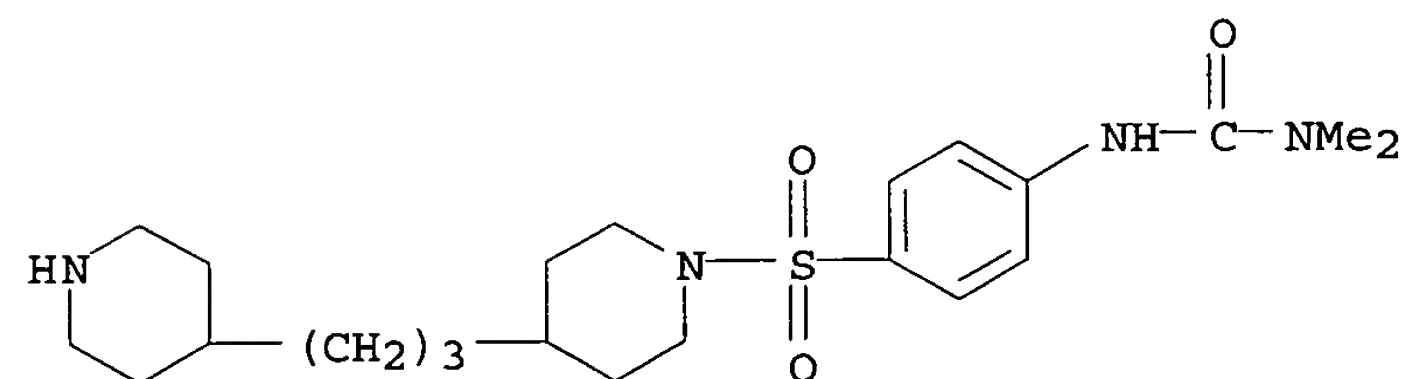
RN 479619-09-5 HCAPLUS

CN Piperidine, 1-[[2-methyl-5-(trifluoromethyl)phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



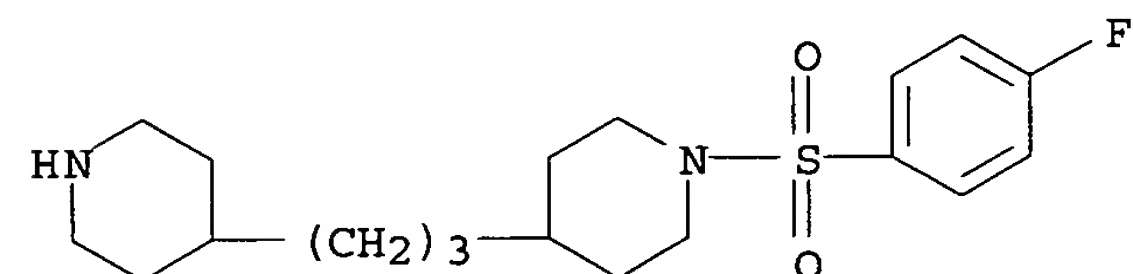
RN 479619-10-8 HCAPLUS

CN Piperidine, 1-[[4-[[[(dimethylamino)carbonyl]amino]phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



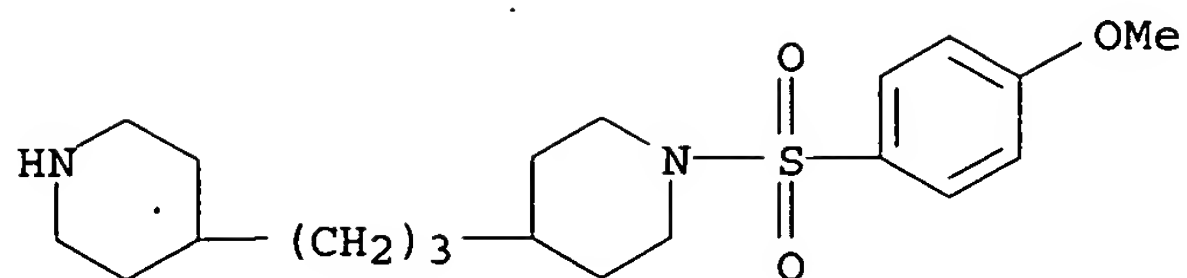
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CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

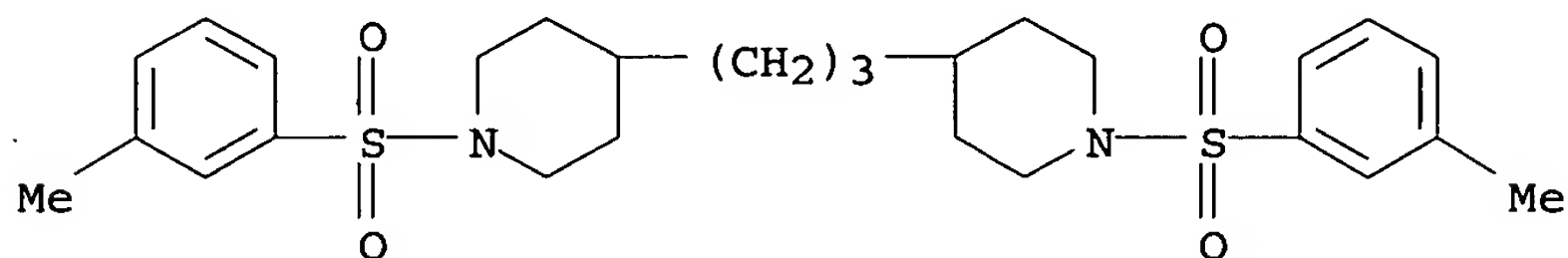


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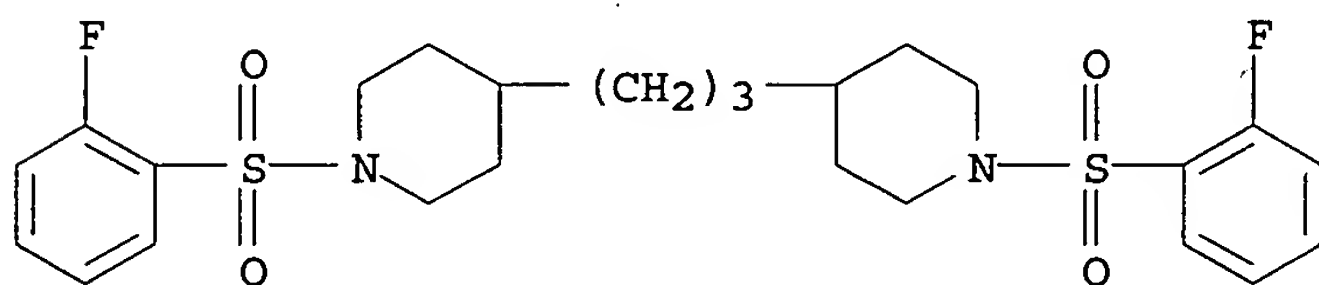
CN Piperidine, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)



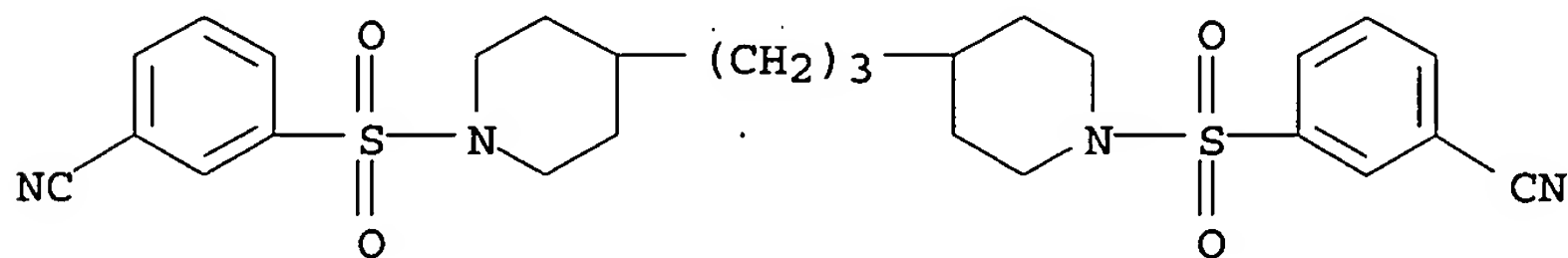
RN 479619-13-1 HCAPLUS

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(CA INDEX NAME)

RN 479619-14-2 HCAPLUS

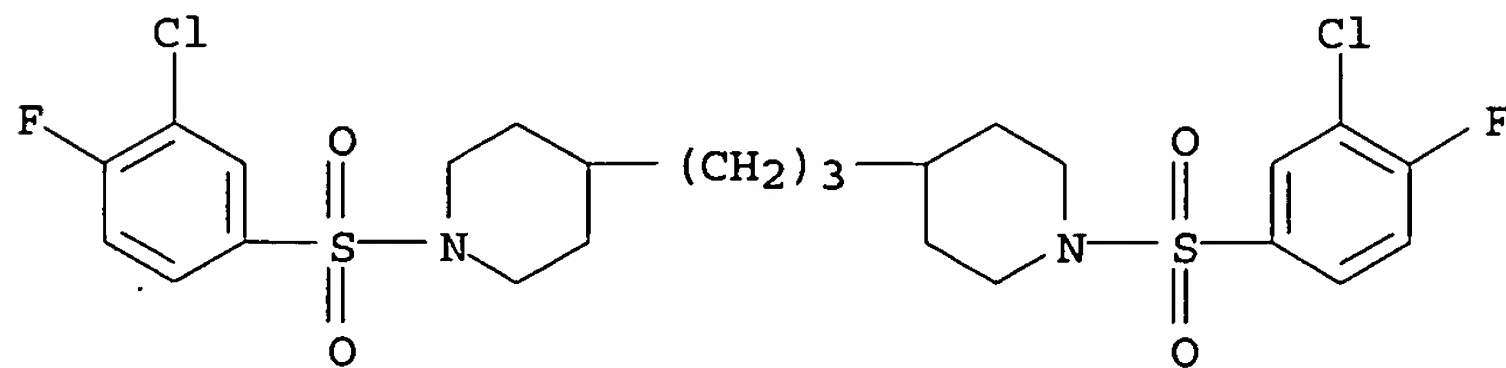
CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(2-fluorophenyl)sulfonyl]- (9CI)  
(CA INDEX NAME)

RN 479619-15-3 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(3-cyanophenyl)sulfonyl]- (9CI)  
(CA INDEX NAME)

RN 479619-16-4 HCAPLUS

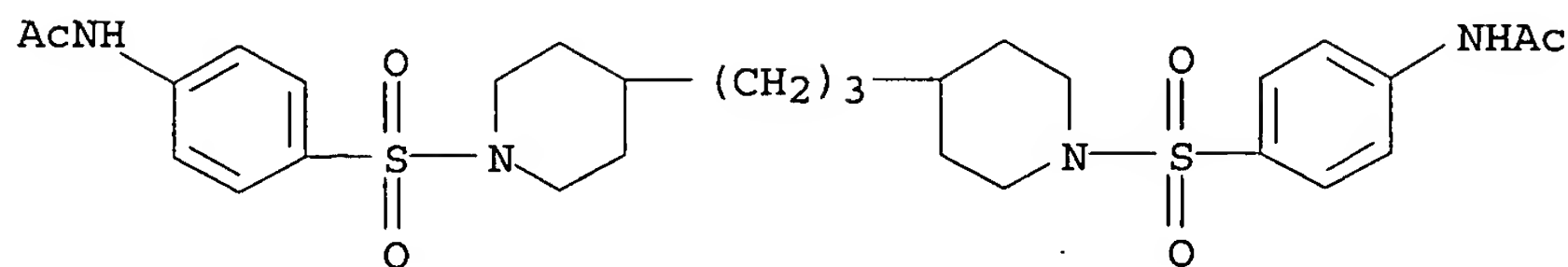
CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 479619-17-5 HCAPLUS

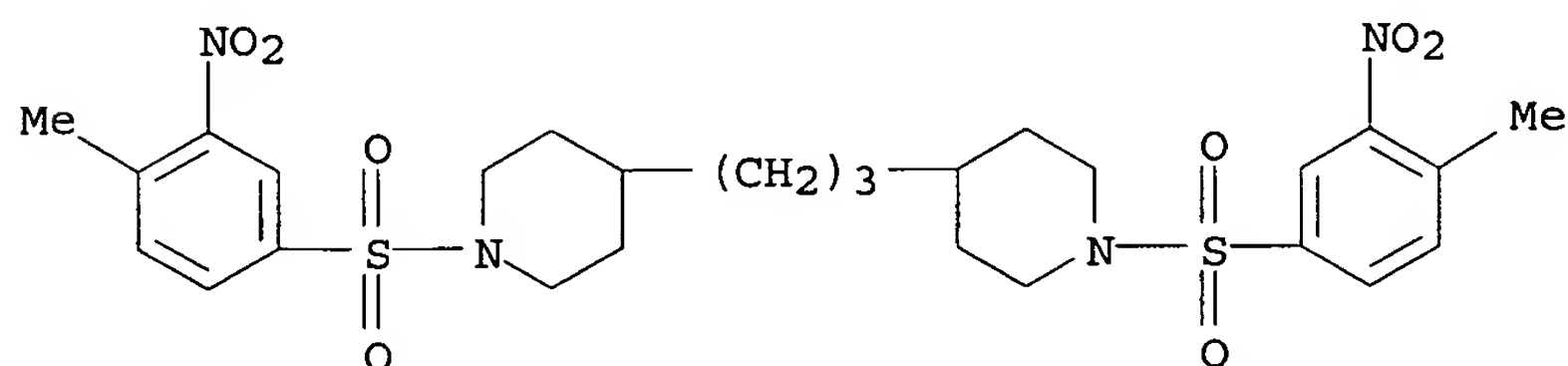
CN Acetamide, N,N'-[1,3-propanediylbis(4,1-piperidinediylsulfonyl)-4,1-

phenylene)]bis- (9CI) (CA INDEX NAME)



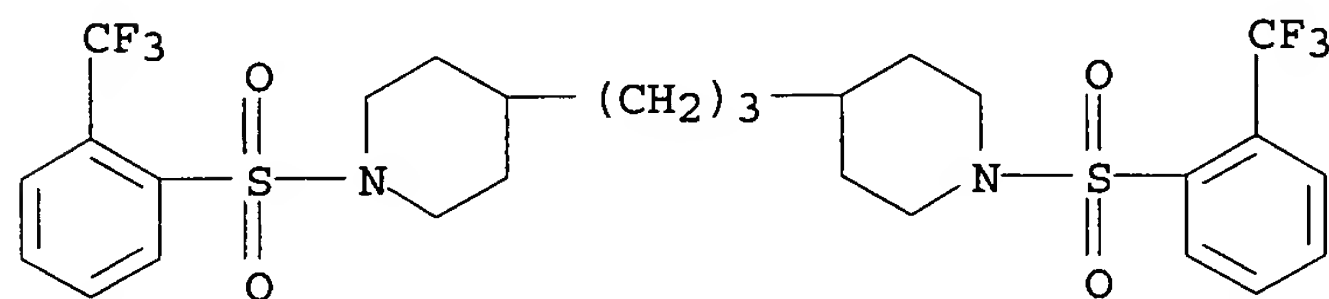
RN 479619-18-6 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-methyl-3-nitrophenyl)sulfonyl]-(9CI) (CA INDEX NAME)



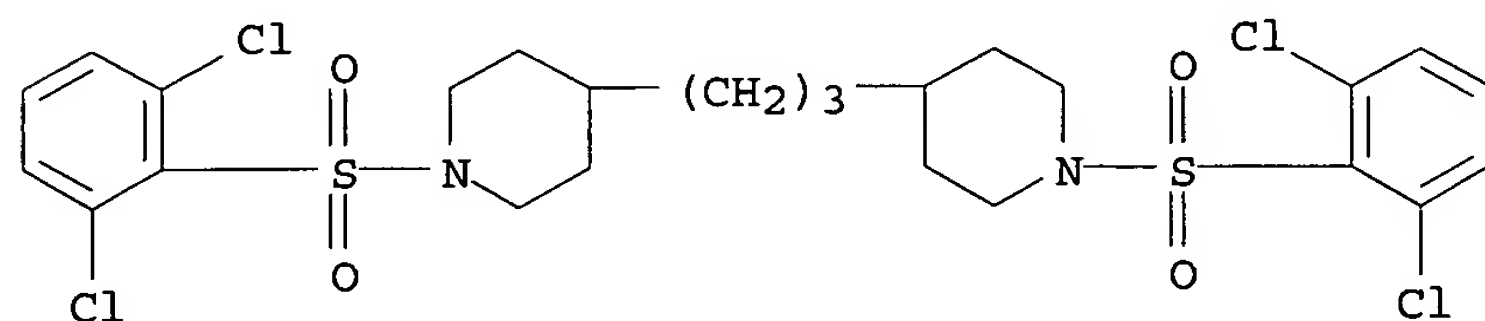
RN 479619-19-7 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[[2-(trifluoromethyl)phenyl]sulfonyl]-(9CI) (CA INDEX NAME)



RN 479619-20-0 HCAPLUS

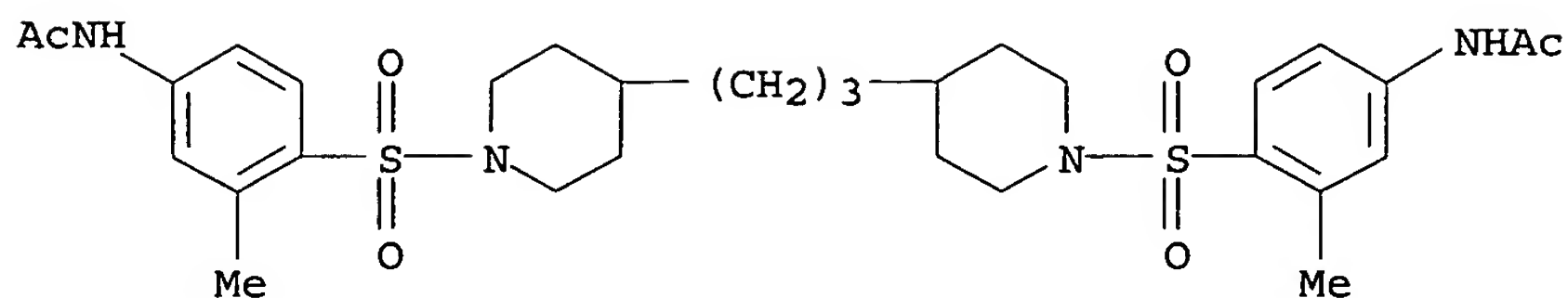
CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(2,6-dichlorophenyl)sulfonyl]-(9CI) (CA INDEX NAME)



RN 479619-21-1 HCAPLUS

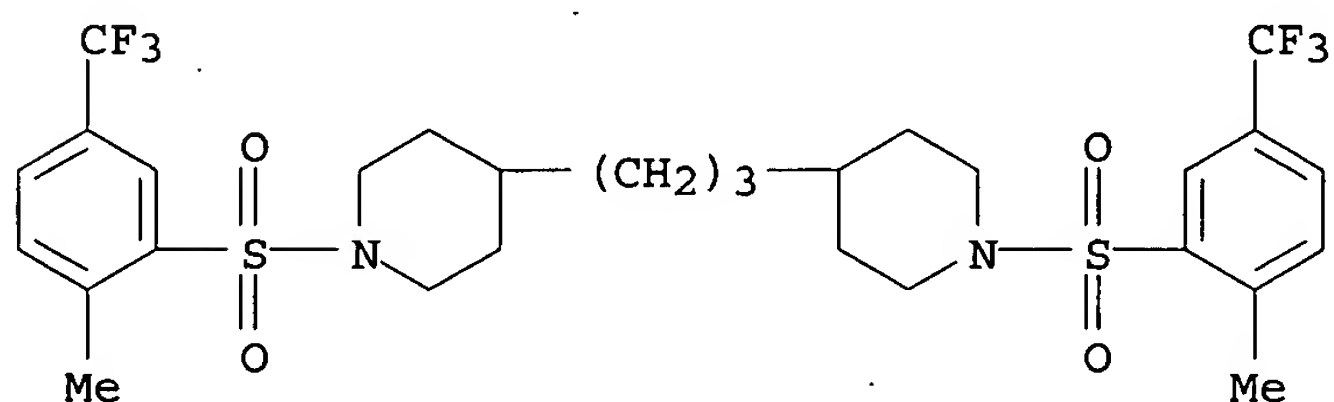
CN Acetamide, N,N'-[1,3-propanediylbis[4,1-piperidinediylsulfonyl(3-methyl-4,1-phenylene)]]bis- (9CI) (CA INDEX NAME)





RN 479619-22-2 HCAPLUS

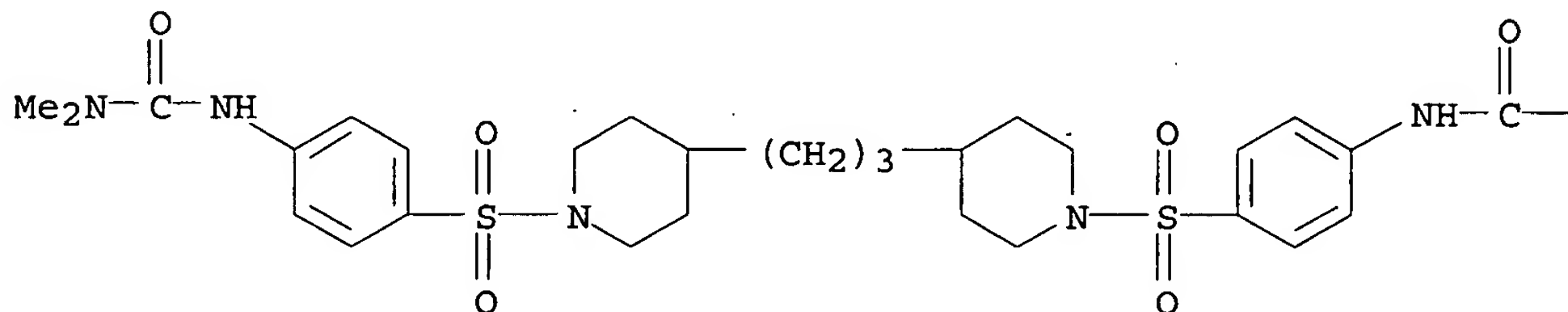
CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[[2-methyl-5-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 479619-23-3 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[[4-[[[(dimethylamino)carbonyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



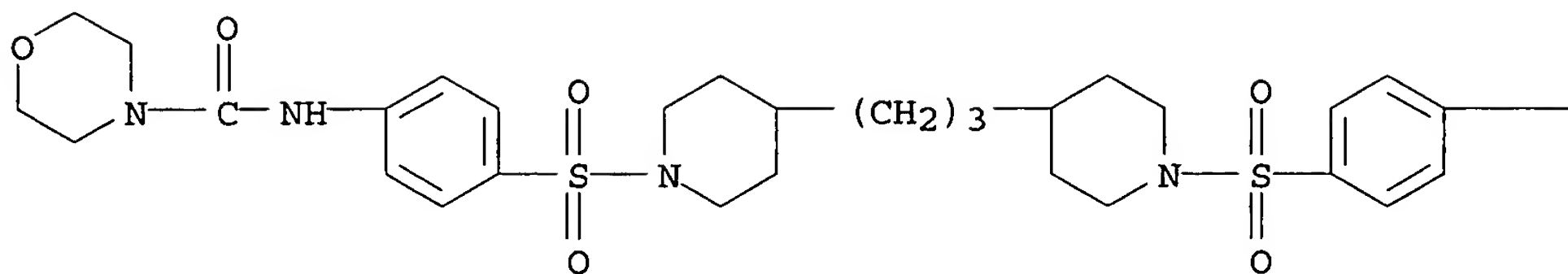
PAGE 1-B

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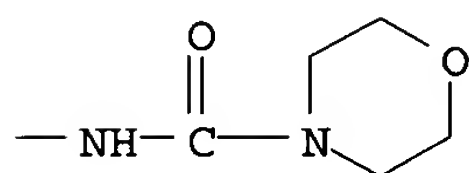
RN 479619-24-4 HCAPLUS

CN 4-Morpholinecarboxamide, N,N'-[1,3-propanediylbis(4,1-piperidinediyl)sulfonyl-4,1-phenylene]]bis- (9CI) (CA INDEX NAME)

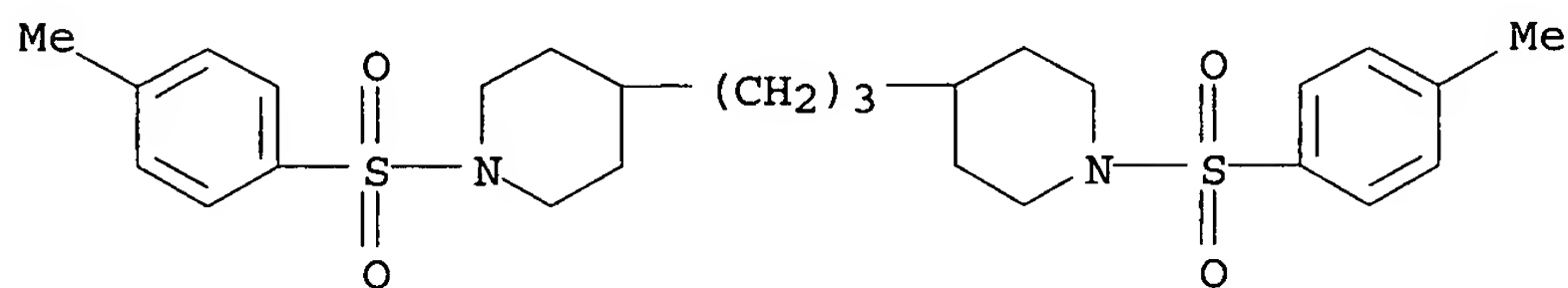
PAGE 1-A



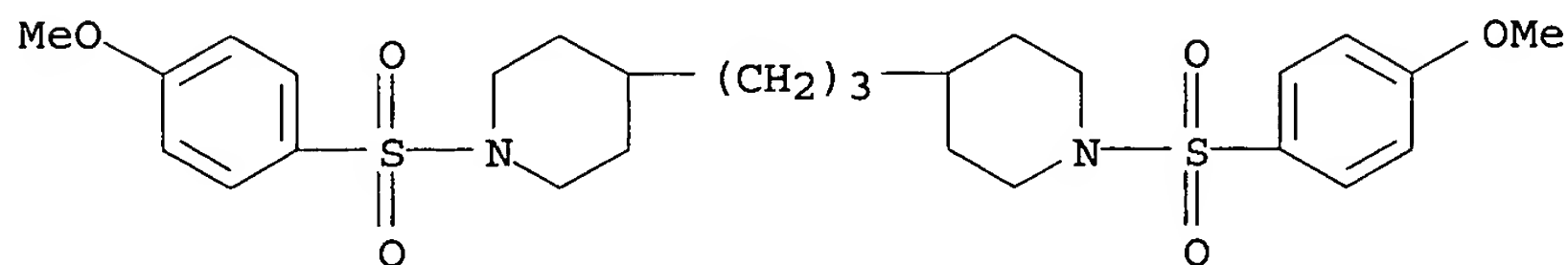
PAGE 1-B



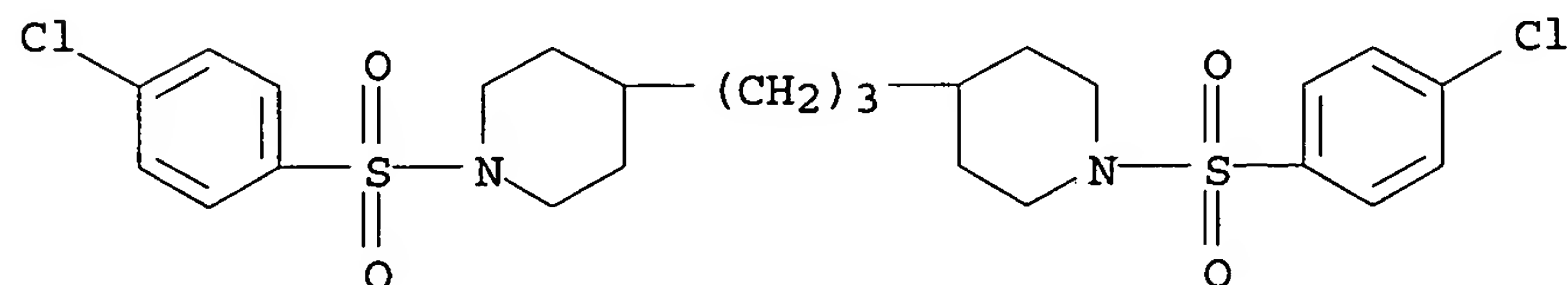
RN 479619-25-5 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-methylphenyl)sulfonyl]]- (9CI)  
(CA INDEX NAME)

RN 479619-26-6 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-methoxyphenyl)sulfonyl]]- (9CI)  
(CA INDEX NAME)

RN 479619-27-7 HCAPLUS

CN Piperidine, 4,4'-(1,3-propanediyl)bis[1-[(4-chlorophenyl)sulfonyl]]- (9CI)  
(CA INDEX NAME)

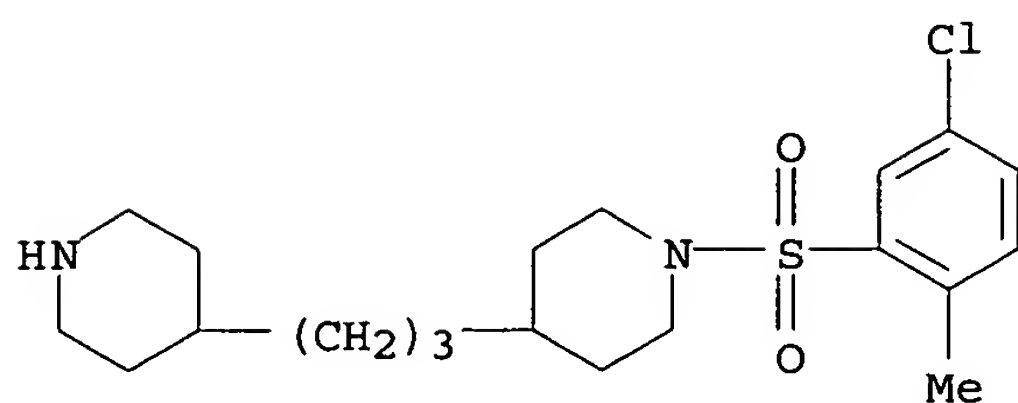
RN 479619-29-9 HCAPLUS

CN Piperidine, 1-[(5-chloro-2-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-28-8

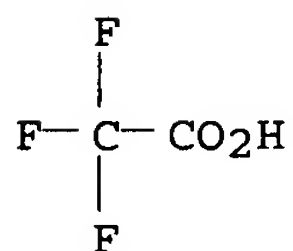
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



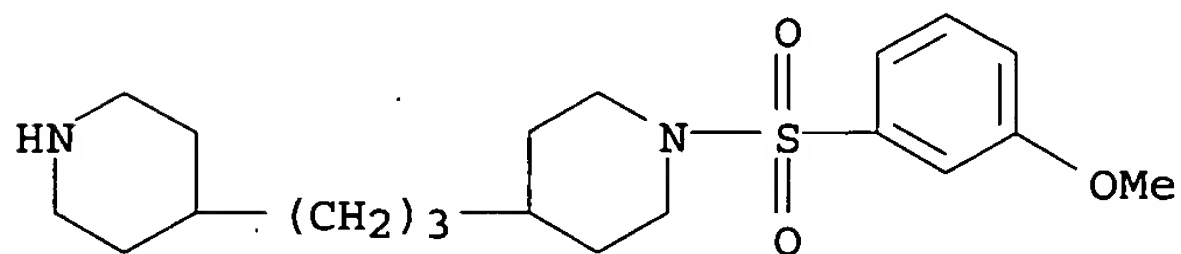
RN 479619-31-3 HCAPLUS

CN Piperidine, 1-[(3-methoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-30-2

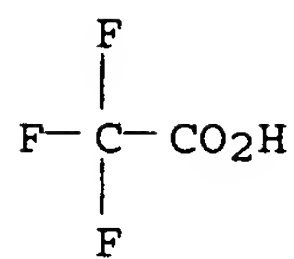
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CM 2

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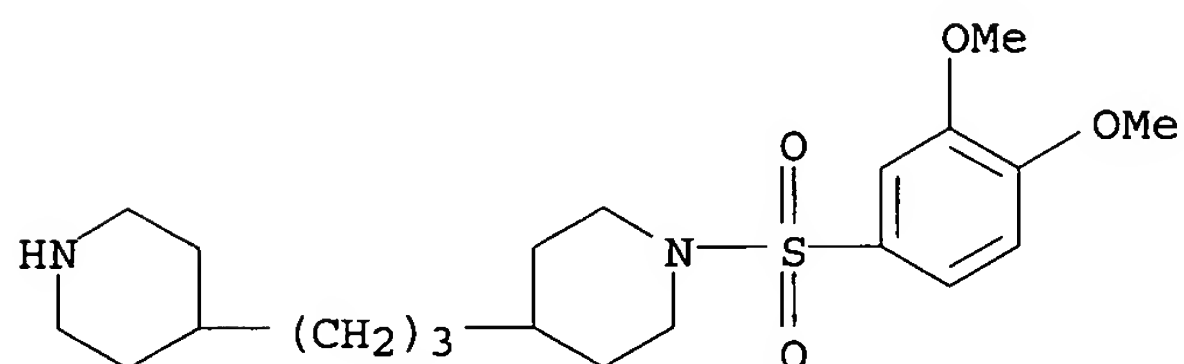
CMF C2 H F3 O2



RN 479619-33-5 HCAPLUS  
 CN Piperidine, 1-[(3,4-dimethoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

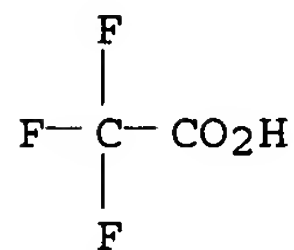
CM 1

CRN 479619-32-4  
 CMF C21 H34 N2 O4 S



CM 2

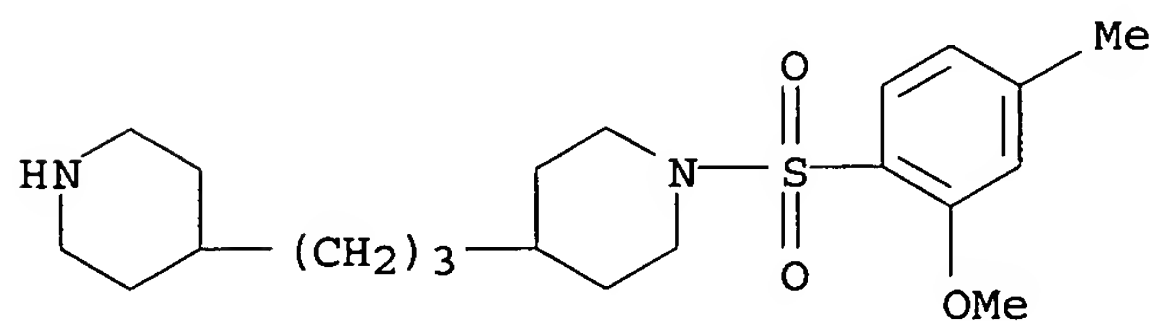
CRN 76-05-1  
 CMF C2 H F3 O2



RN 479619-35-7 HCAPLUS  
 CN Piperidine, 1-[(2-methoxy-4-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

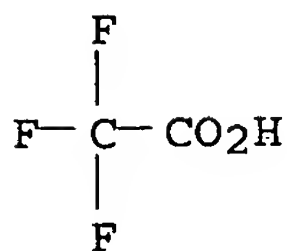
CRN 479619-34-6  
 CMF C21 H34 N2 O3 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



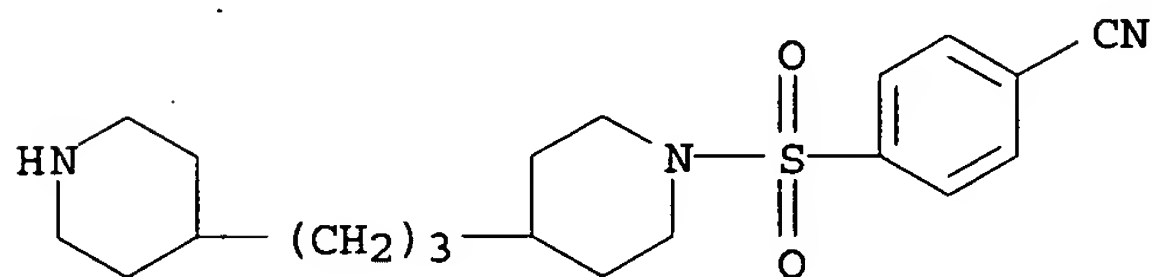
RN 479619-37-9 HCAPLUS

CN Piperidine, 1-[(4-cyanophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-36-8

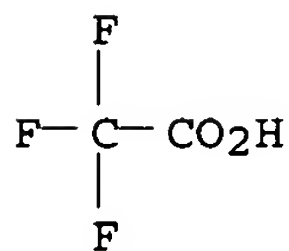
CMF C20 H29 N3 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



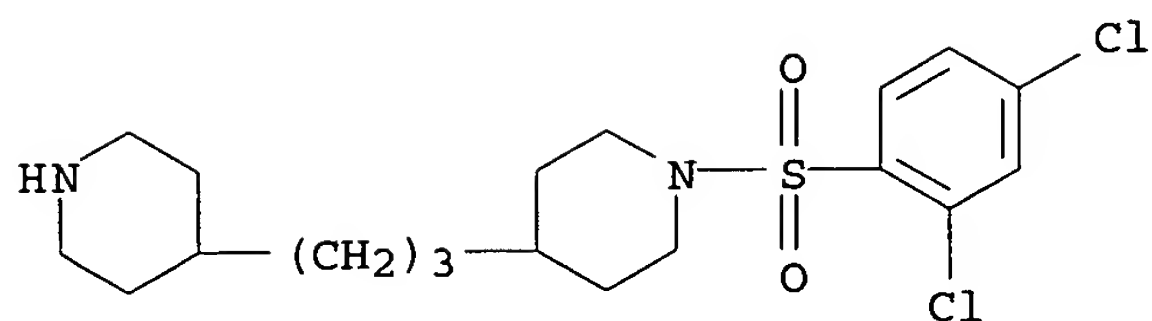
RN 479619-39-1 HCAPLUS

CN Piperidine, 1-[(2,4-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-38-0

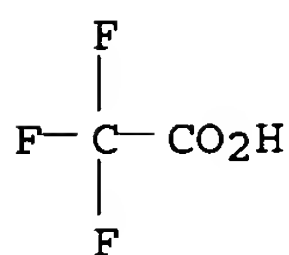
CMF C19 H28 Cl2 N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



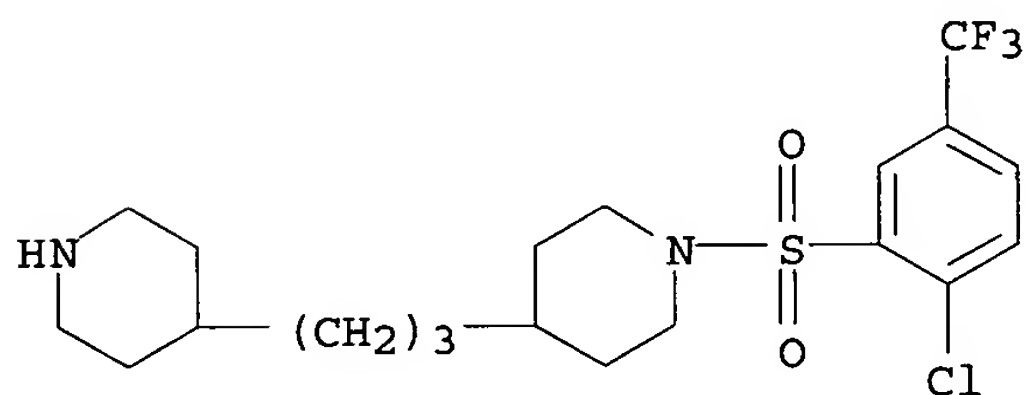
RN 479619-41-5 HCAPLUS

CN Piperidine, 1-[[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-40-4

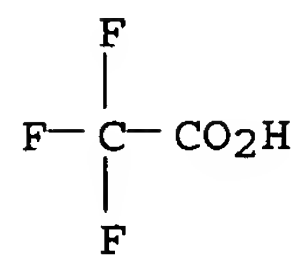
CMF C20 H28 Cl F3 N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 479619-43-7 HCAPLUS

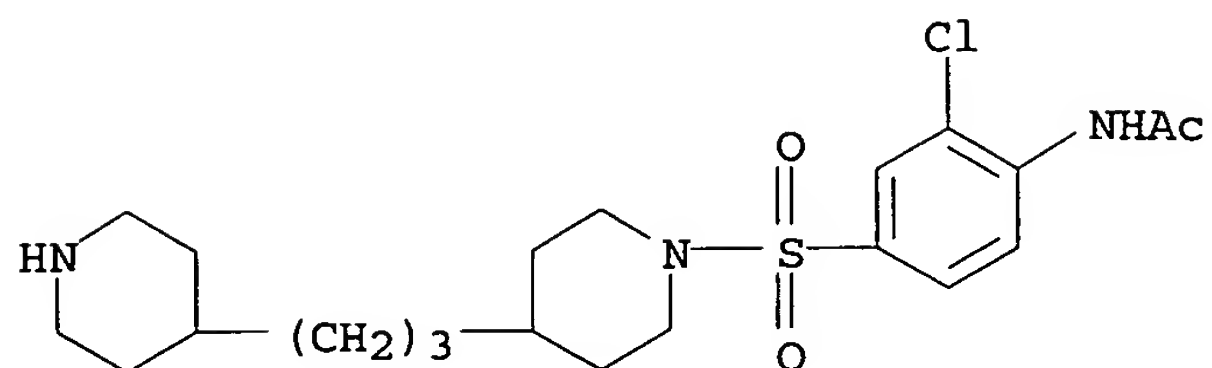
CN Acetamide, N-[2-chloro-4-[[4-[3-(4-piperidinyl)propyl]-1-piperidinyl]sulfonyl]phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

NAME)

CM 1

CRN 479619-42-6

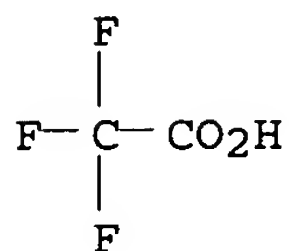
CMF C21 H32 Cl N3 O3 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



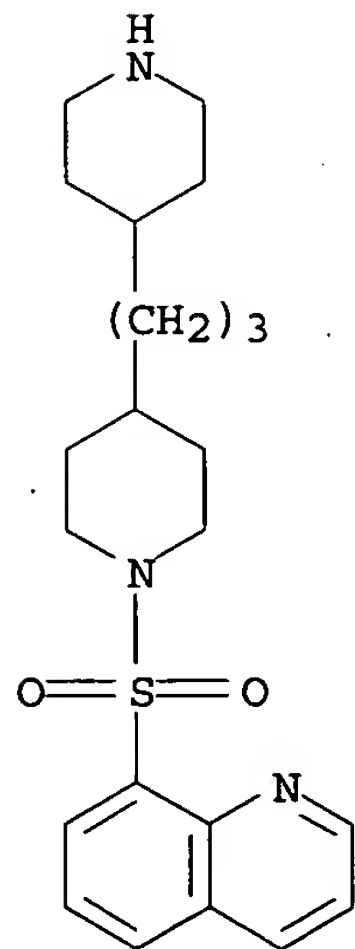
RN 479619-45-9 HCAPLUS

CN Piperidine, 4-[3-(4-piperidinyl)propyl]-1-(8-quinolinylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

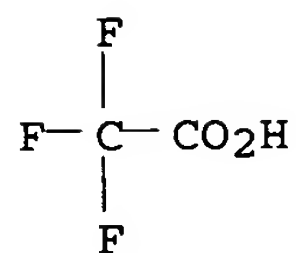
CRN 479619-44-8

CMF C22 H31 N3 O2 S



CM 2

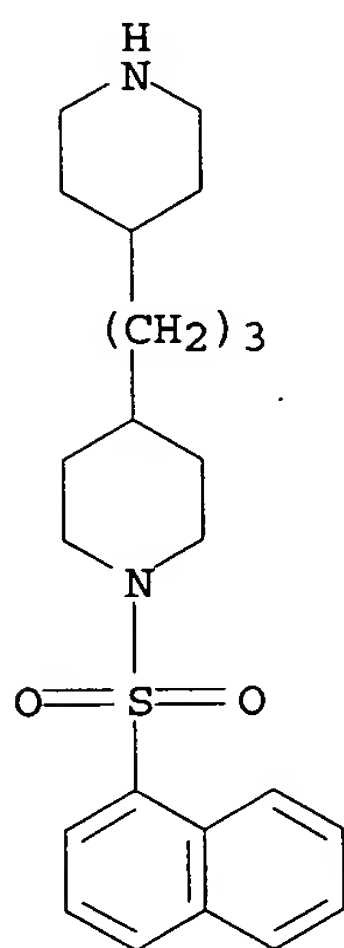
CRN 76-05-1  
CMF C2 H F3 O2



RN 479619-47-1 HCAPLUS  
CN Piperidine, 1-(1-naphthalenylsulfonyl)-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

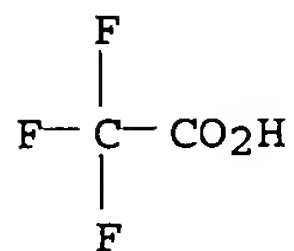
CM 1

CRN 479619-46-0  
CMF C23 H32 N2 O2 S



CM 2

CRN 76-05-1  
CMF C2 H F3 O2



RN 479619-49-3 HCAPLUS

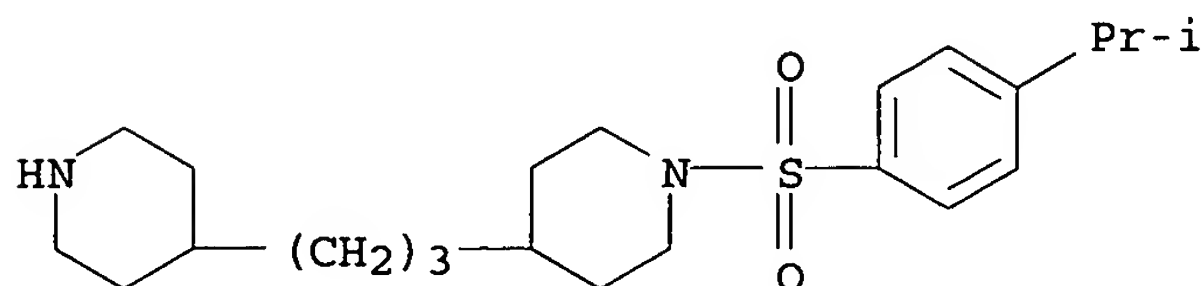


CN Piperidine, 1-[[4-(1-methylethyl)phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-48-2

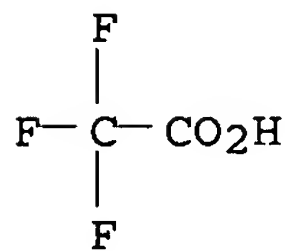
CMF C22 H36 N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



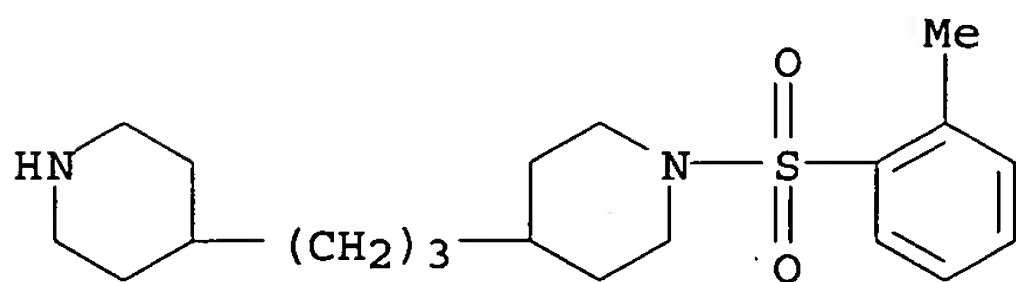
RN 479619-51-7 HCAPLUS

CN Piperidine, 1-[(2-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-50-6

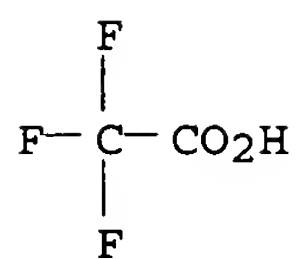
CMF C20 H32 N2 O2 S



CM 2

CRN 76-05-1

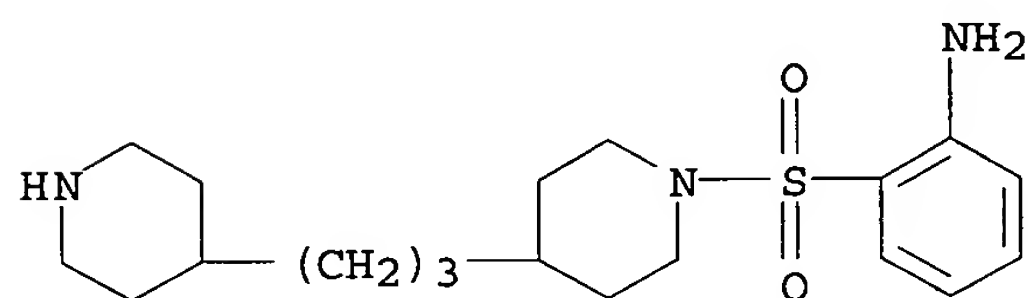
CMF C20 H32 N2 O2 S



RN 479619-53-9 HCAPLUS  
 CN Piperidine, 1-[(2-aminophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

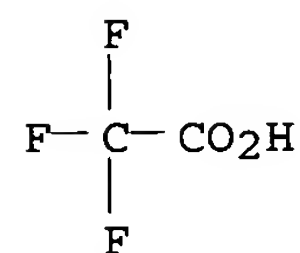
CM 1

CRN 479619-52-8  
 CMF C19 H31 N3 O2 S



CM 2

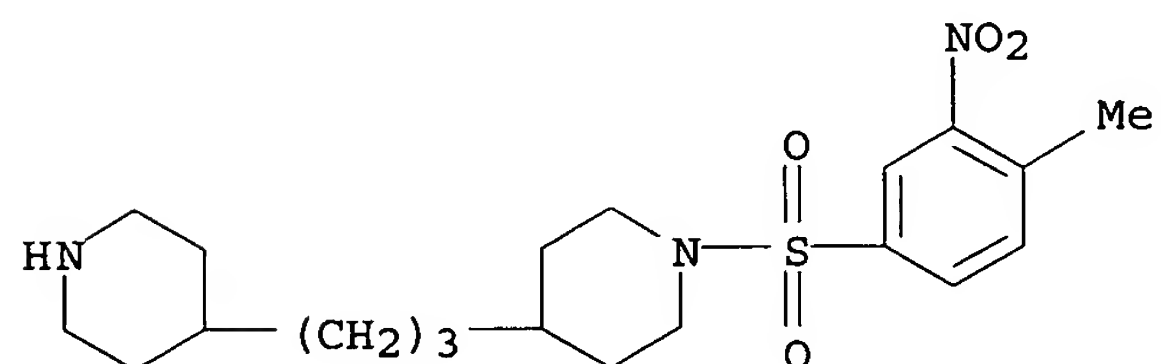
CRN 76-05-1  
 CMF C2 H F3 O2



RN 479619-54-0 HCAPLUS  
 CN Piperidine, 1-[(4-methyl-3-nitrophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

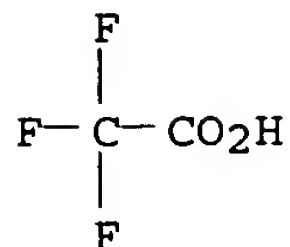
CRN 479619-04-0  
 CMF C20 H31 N3 O4 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



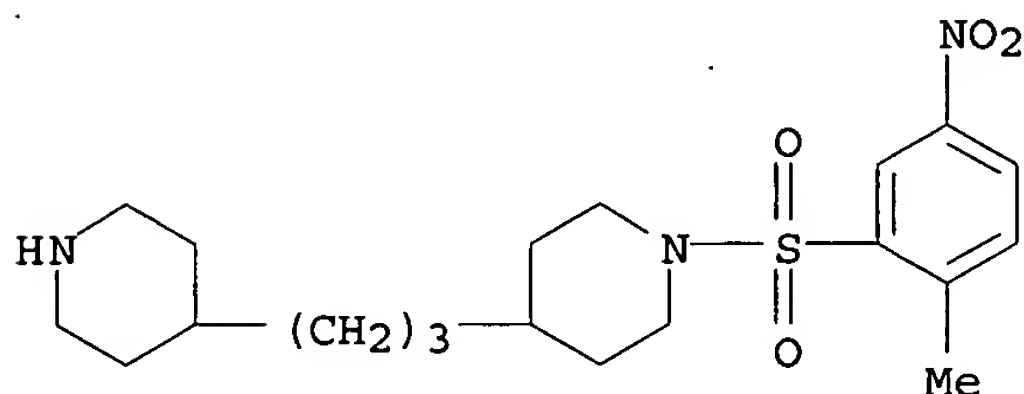
RN 479619-57-3 HCAPLUS

CN Piperidine, 1-[(2-methyl-5-nitrophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-56-2

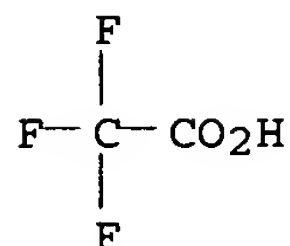
CMF C20 H31 N3 O4 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



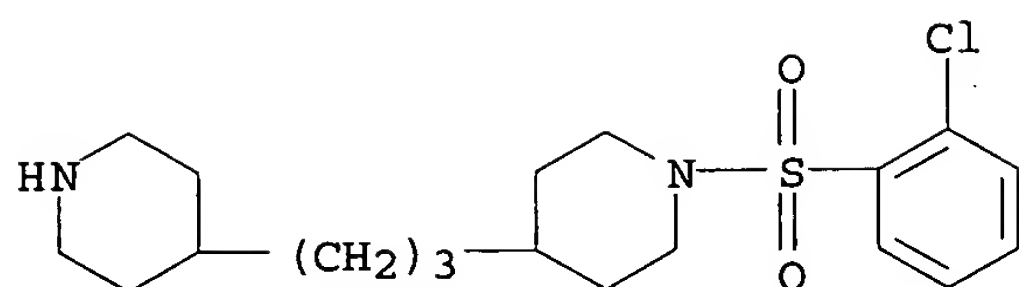
RN 479619-60-8 HCAPLUS

CN Piperidine, 1-[(2-chlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-59-5

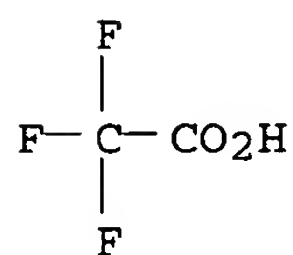
CMF C19 H29 Cl N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



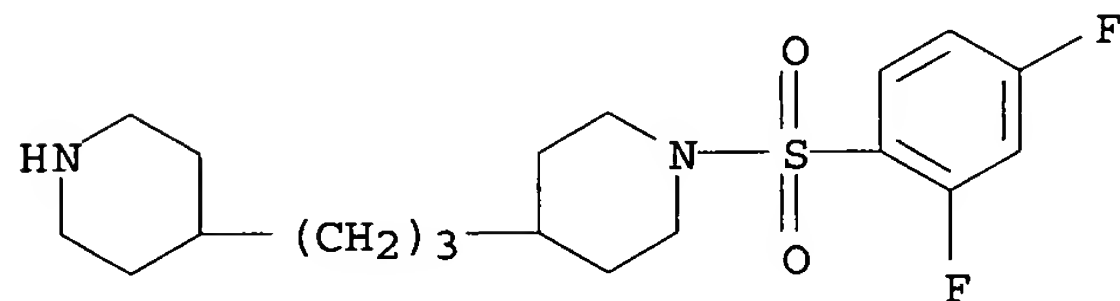
RN 479619-63-1 HCAPLUS

CN Piperidine, 1-[(2,4-difluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-62-0

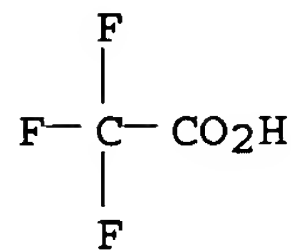
CMF C19 H28 F2 N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2

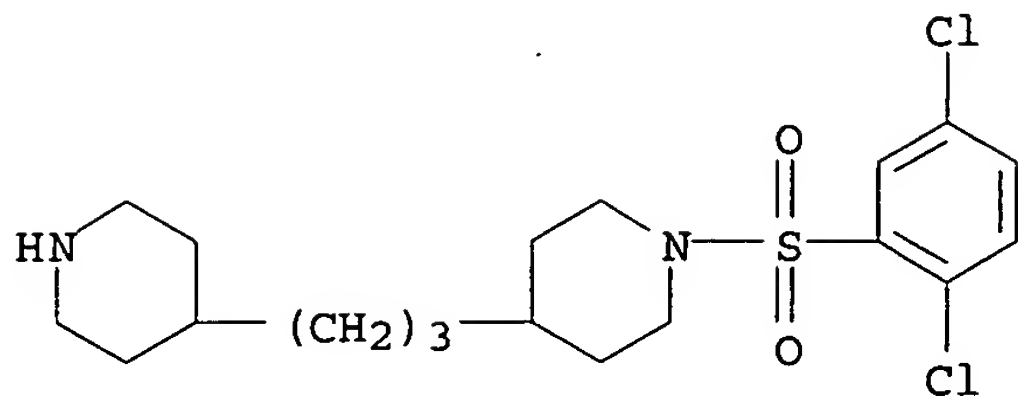


RN 479619-66-4 HCAPLUS

CN Piperidine, 1-[(2,5-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

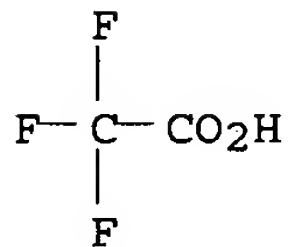
CM 1

CRN 479619-65-3  
CMF C19 H28 Cl2 N2 O2 S



CM 2

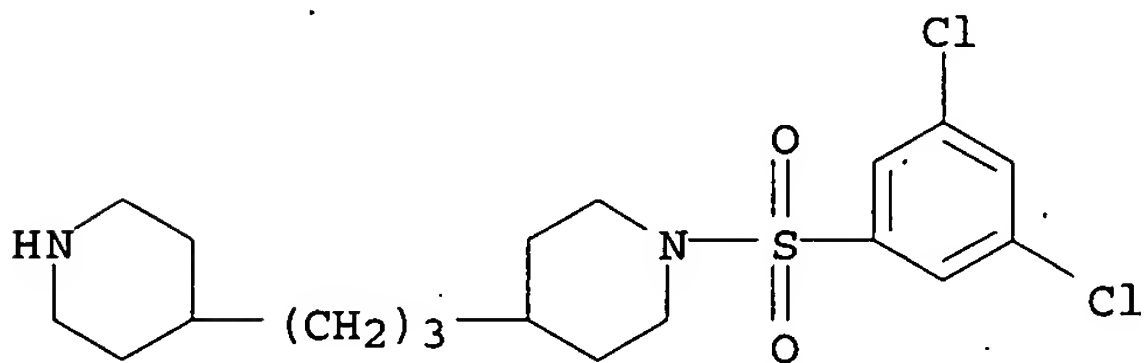
CRN 76-05-1  
CMF C2 H F3 O2



RN 479619-69-7 HCAPLUS  
CN Piperidine, 1-[(3,5-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

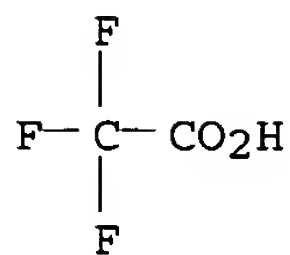
CM 1

CRN 479619-68-6  
CMF C19 H28 Cl2 N2 O2 S



CM 2

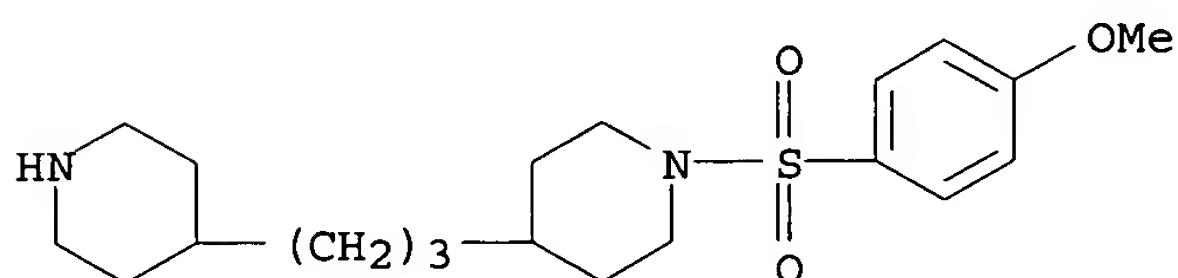
CRN 76-05-1  
CMF C2 H F3 O2



RN 479619-71-1 HCAPLUS  
 CN Piperidine, 1-[(4-methoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

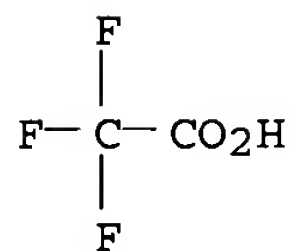
CM 1

CRN 479619-12-0  
 CMF C20 H32 N2 O3 S



CM 2

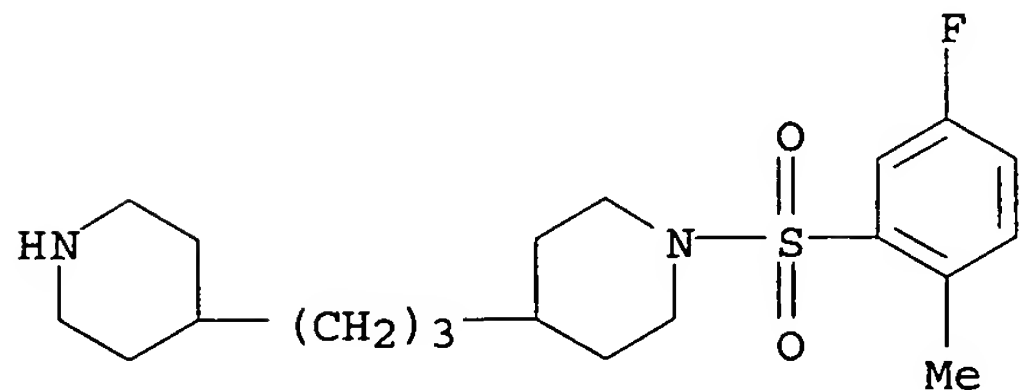
CRN 76-05-1  
 CMF C2 H F3 O2



RN 479619-74-4 HCAPLUS  
 CN Piperidine, 1-[(5-fluoro-2-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

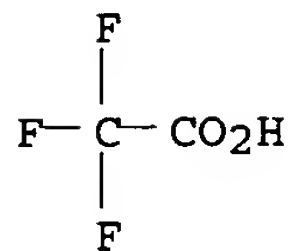
CRN 479619-73-3  
 CMF C20 H31 F N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



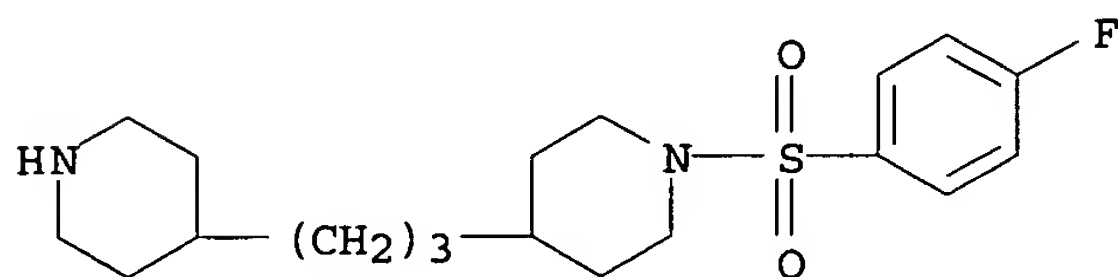
RN 479619-76-6 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-11-9

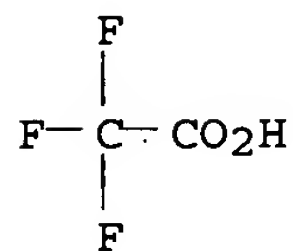
CMF C19 H29 F N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



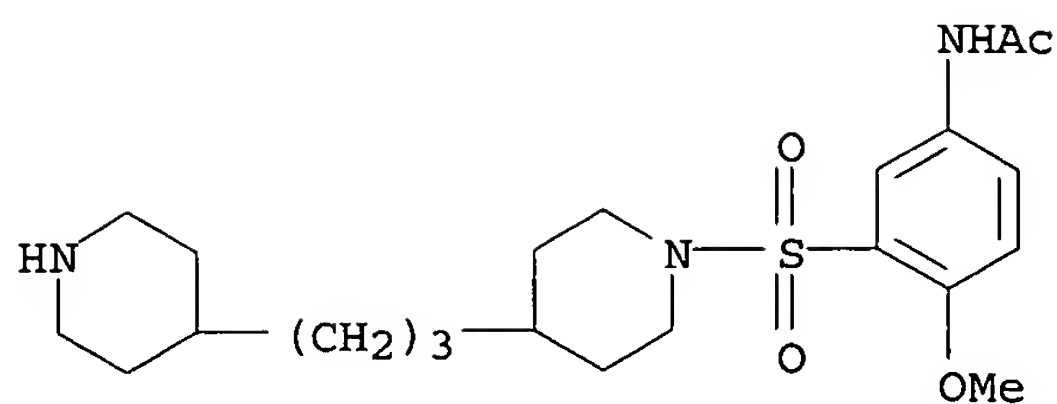
RN 479619-79-9 HCAPLUS

CN Acetamide, N-[4-methoxy-3-[[4-[3-(4-piperidinyl)propyl]-1-piperidinyl]sulfonyl]phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-78-8

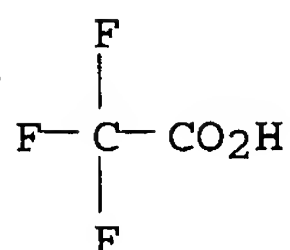
CMF C22 H35 N3 O4 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



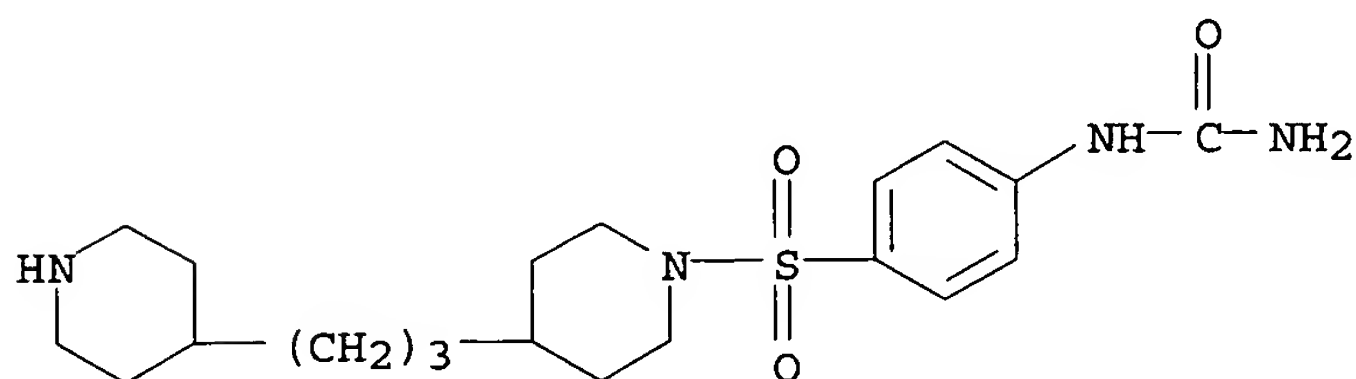
RN 479619-82-4 HCAPLUS

CN Piperidine, 1-[[4-[(aminocarbonyl)amino]phenyl]sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-81-3

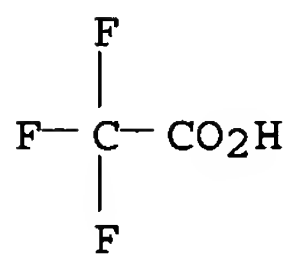
CMF C20 H32 N4 O3 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 479619-85-7 HCAPLUS

CN Piperidine, 1-[(2-chloro-4-fluorophenyl)sulfonyl]-4-[3-(4-

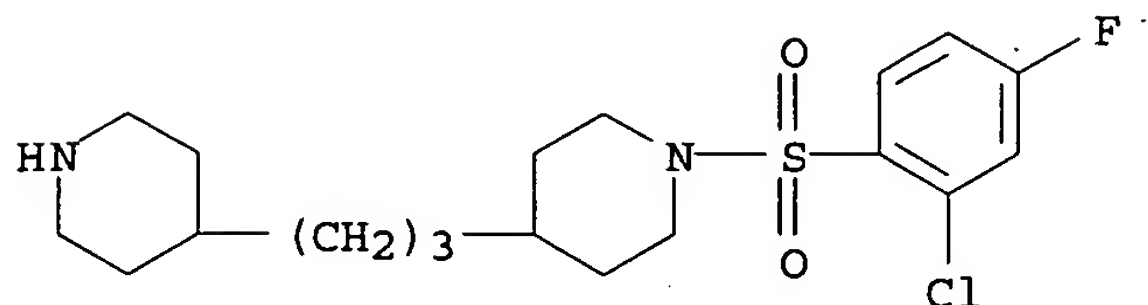


piperidiny]propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-84-6

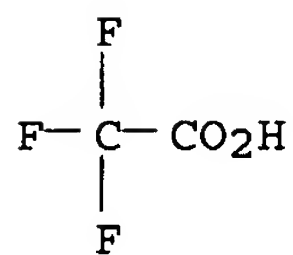
CMF C19 H28 Cl F N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



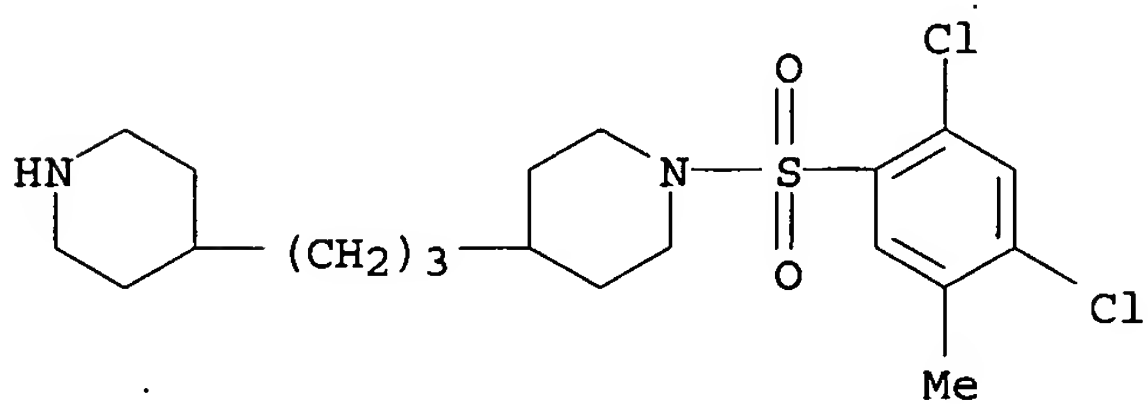
RN 479619-88-0 HCAPLUS

CN Piperidine, 1-[(2,4-dichloro-5-methylphenyl)sulfonyl]-4-[3-(4-piperidiny]propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-87-9

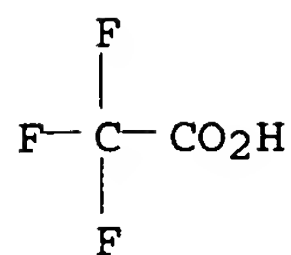
CMF C20 H30 Cl2 N2 O2 S



CM 2

CRN 76-05-1

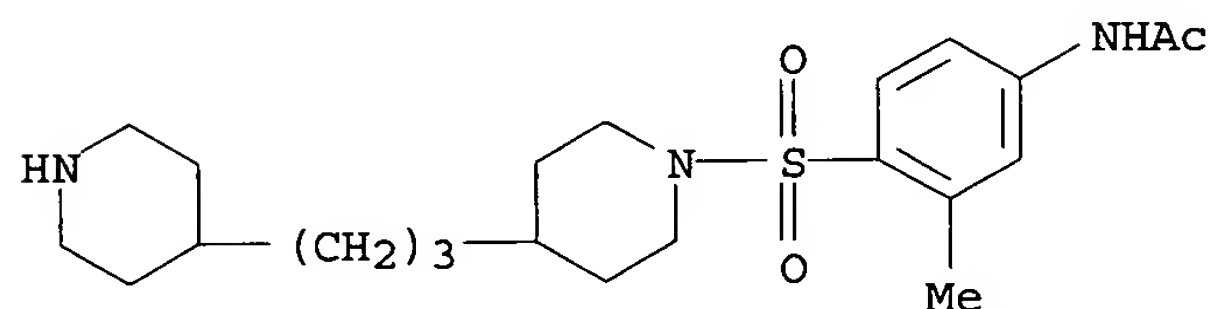
CMF C2 H F3 O2



RN 479619-90-4 HCAPLUS  
 CN Acetamide, N-[3-methyl-4-[[4-[3-(4-piperidinyl)propyl]-1-piperidinyl]sulfonyl]phenyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

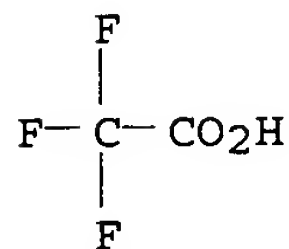
CM 1

CRN 479619-08-4  
 CMF C22 H35 N3 O3 S



CM 2

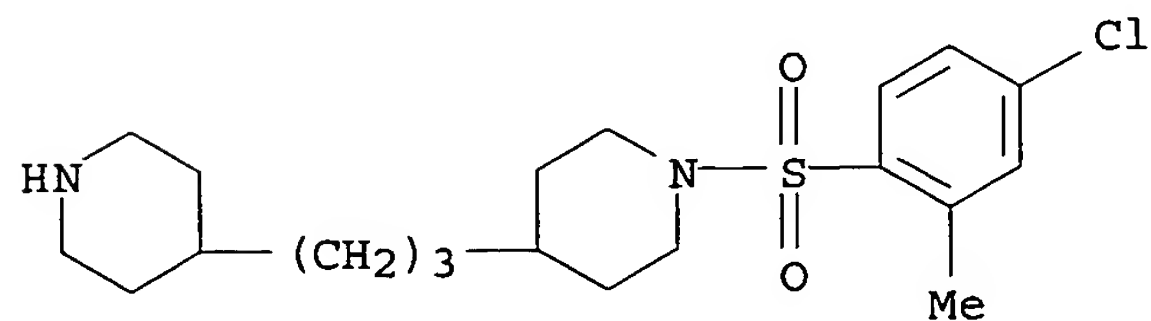
CRN 76-05-1  
 CMF C2 H F3 O2



RN 479619-93-7 HCAPLUS  
 CN Piperidine, 1-[(4-chloro-2-methylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

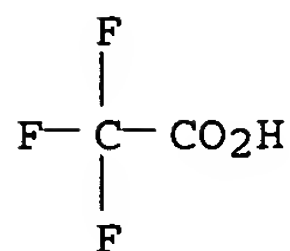
CRN 479619-92-6  
 CMF C20 H31 Cl N2 O2 S



CM 2

CRN 76-05-1

CMF C2 H F3 O2



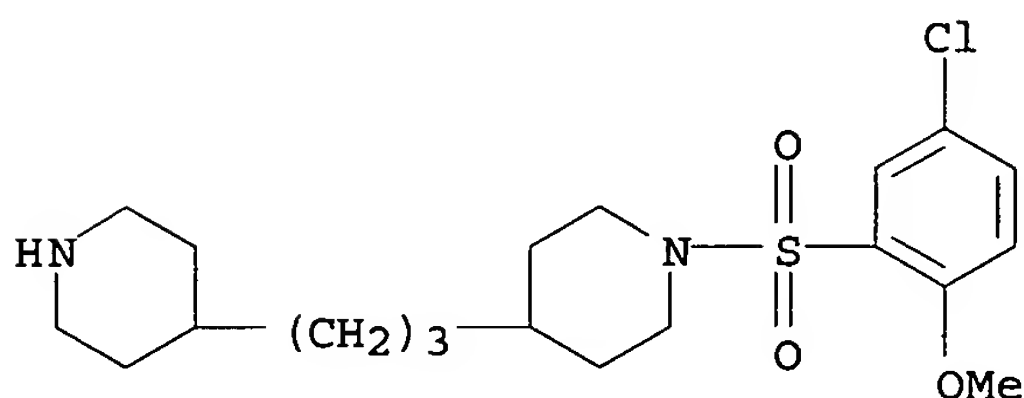
RN 479619-96-0 HCAPLUS

CN Piperidine, 1-[(5-chloro-2-methoxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 479619-95-9

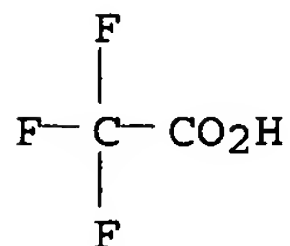
CMF C20 H31 Cl N2 O3 S



CM 2

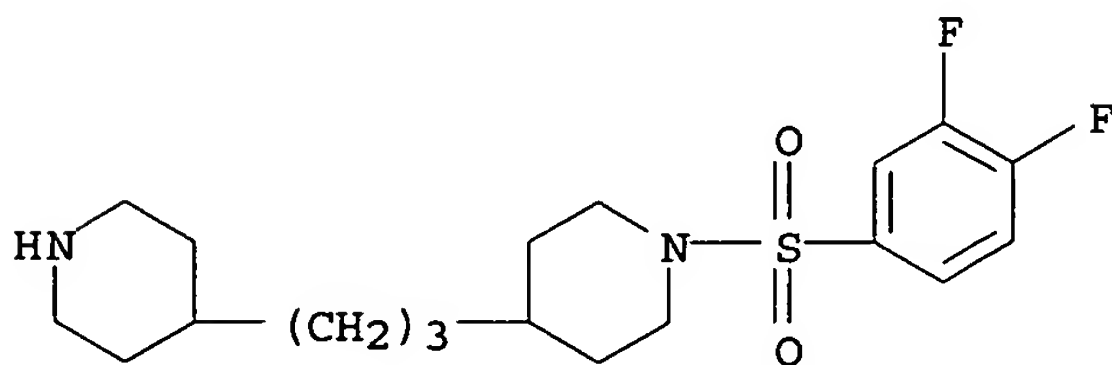
CRN 76-05-1

CMF C2 H F3 O2

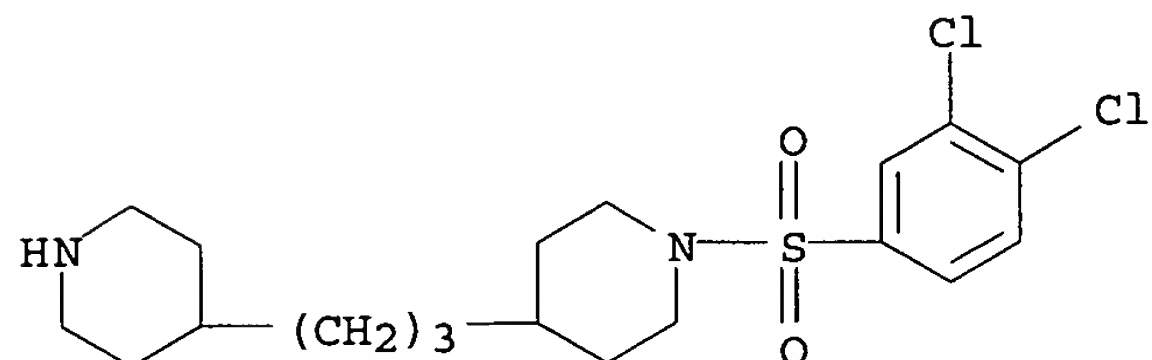


RN 479619-98-2 HCAPLUS

CN Piperidine, 1-[(3,4-difluorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

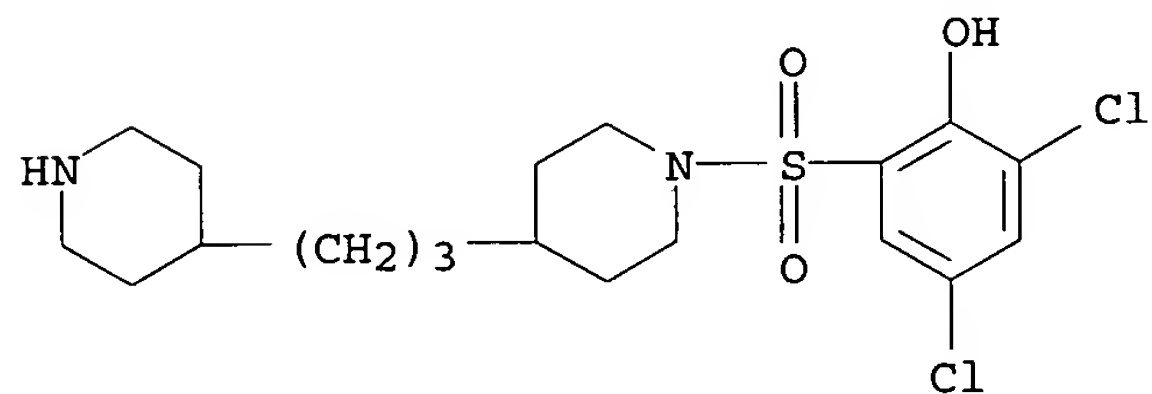


RN 479620-00-3 HCAPLUS

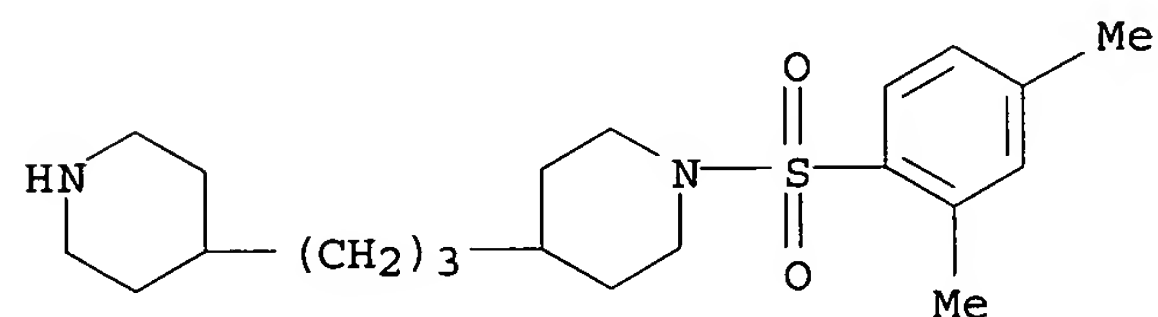
CN Piperidine, 1-[(3,4-dichlorophenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-  
(9CI) (CA INDEX NAME)

RN 479620-02-5 HCAPLUS

CN Piperidine, 1-[(3,5-dichloro-2-hydroxyphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]- (9CI) (CA INDEX NAME)

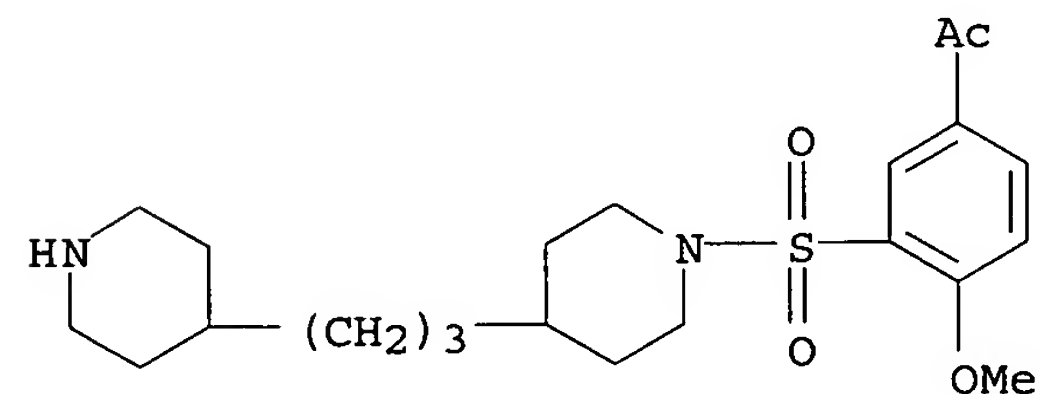


RN 479620-03-6 HCAPLUS

CN Piperidine, 1-[(2,4-dimethylphenyl)sulfonyl]-4-[3-(4-piperidinyl)propyl]-  
(9CI) (CA INDEX NAME)

RN 479620-04-7 HCAPLUS

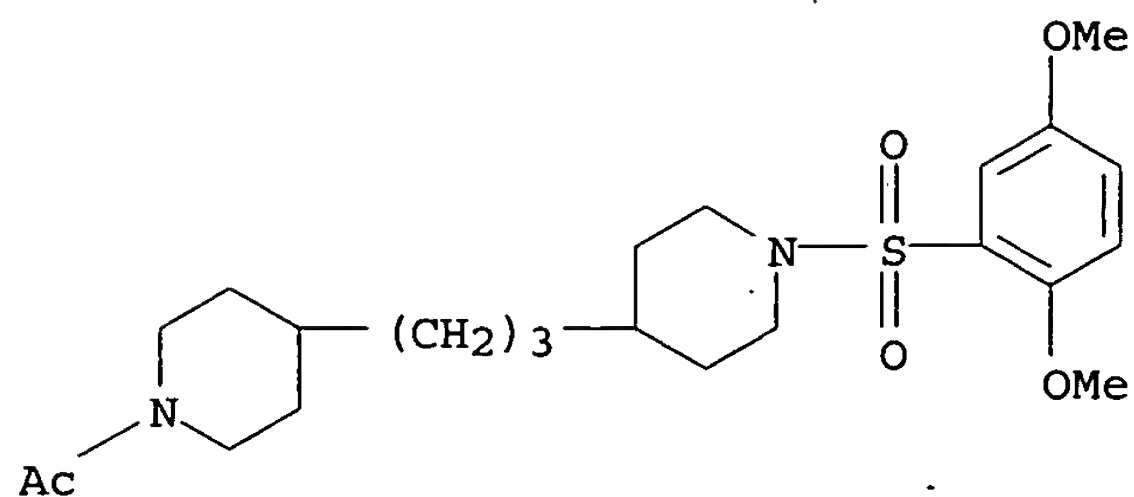
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RN 479620-05-8 HCAPLUS

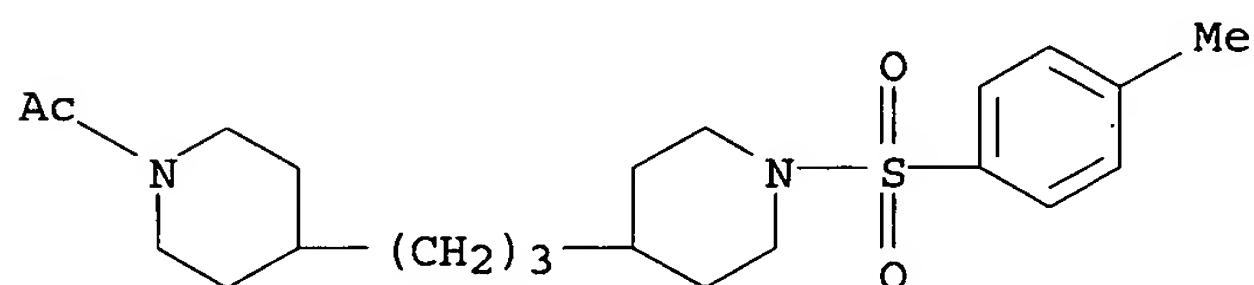
CN Piperidine, 1-acetyl-4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-

piperidinyl]propyl]- (9CI) (CA INDEX NAME)



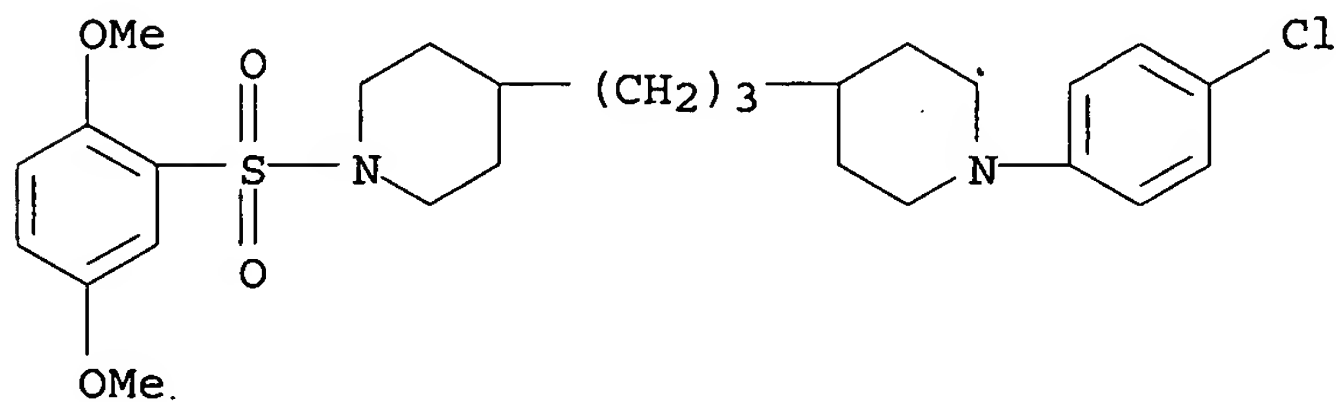
RN 479620-06-9 HCAPLUS

CN Piperidine, 1-acetyl-4-[3-[1-[(4-methylphenyl)sulfonyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)



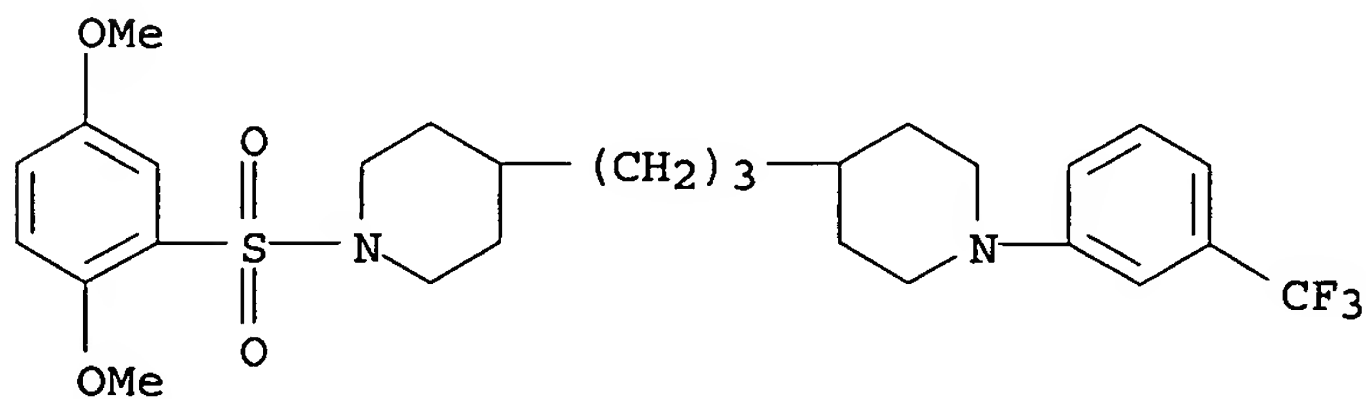
RN 479620-08-1 HCAPLUS

CN Piperidine, 4-[3-[1-(4-chlorophenyl)-4-piperidinyl]propyl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 479620-10-5 HCAPLUS

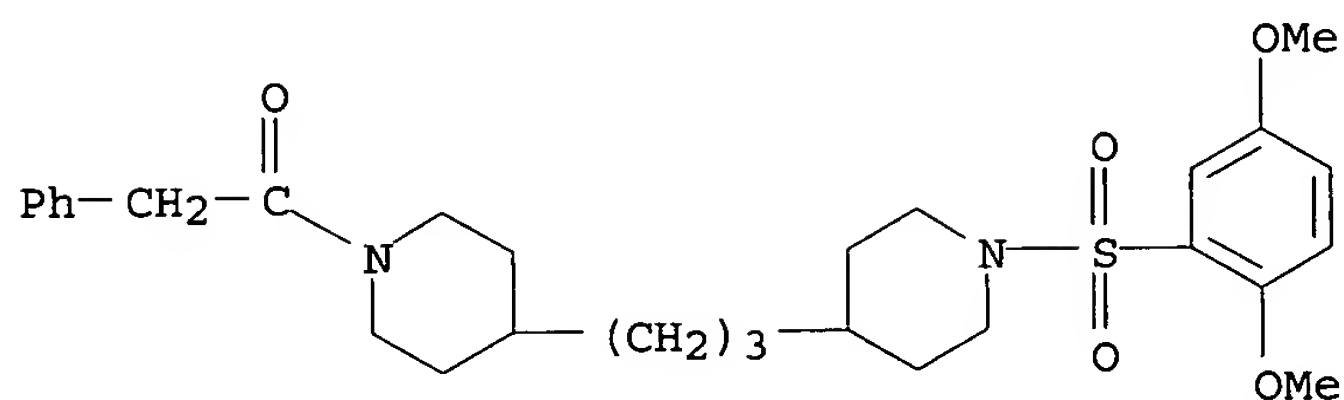
CN Piperidine, 1-[(2,5-dimethoxyphenyl)sulfonyl]-4-[3-[1-[3-(trifluoromethyl)phenyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)



RN 479620-12-7 HCAPLUS

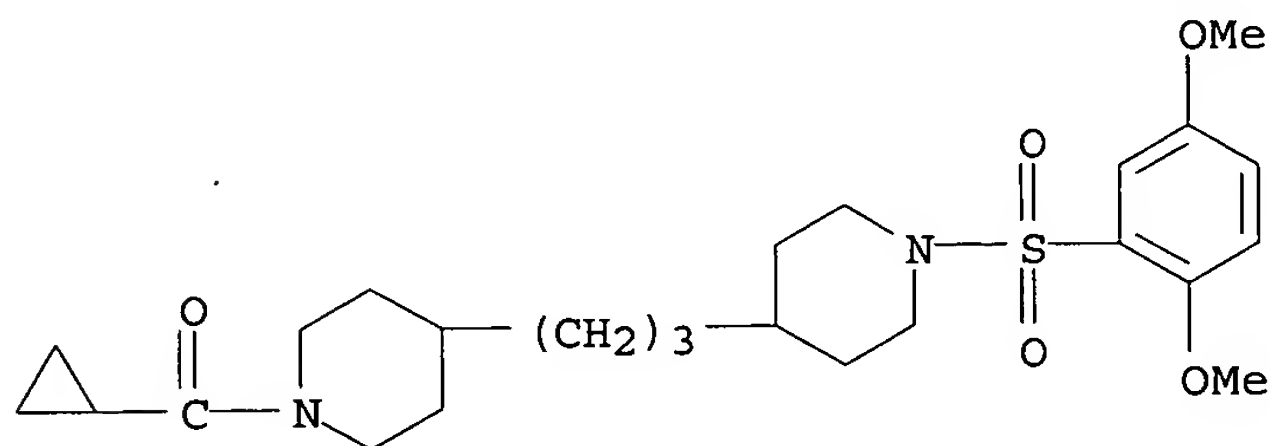
CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-

1-(phenylacetyl)- (9CI) (CA INDEX NAME)



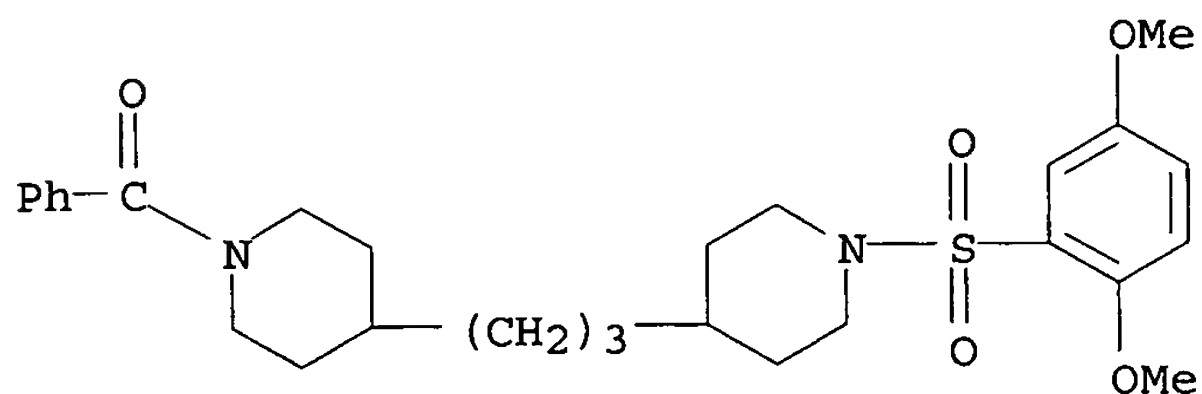
RN 479620-15-0 HCAPLUS

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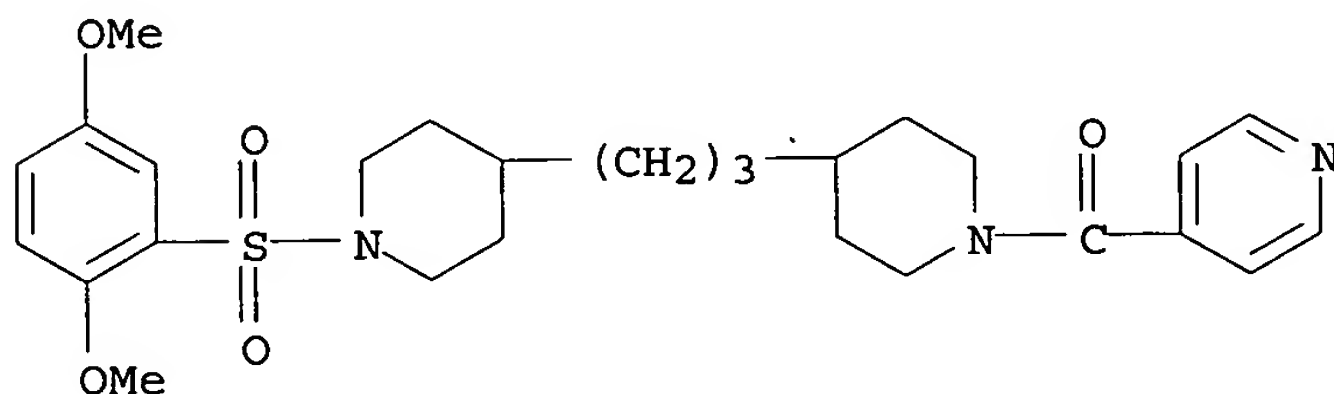
RN 479620-16-1 HCAPLUS

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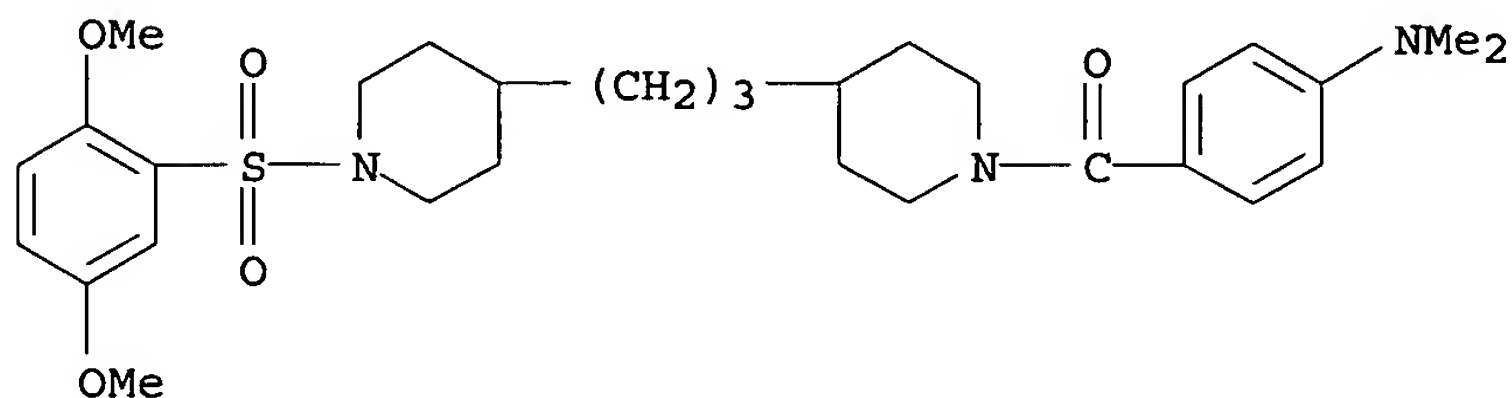
RN 479620-17-2 HCAPLUS

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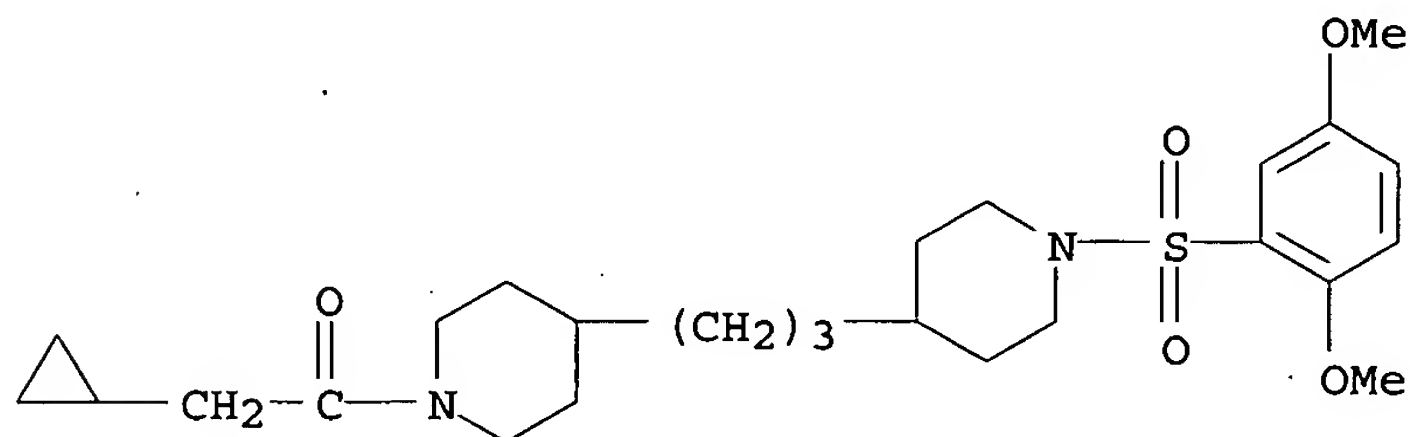
RN 479620-18-3 HCAPLUS

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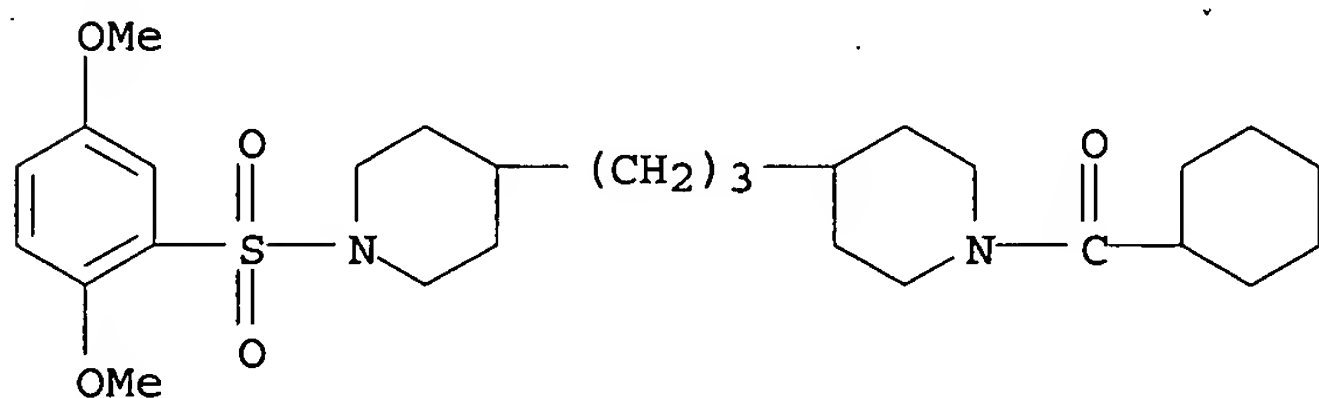
RN 479620-19-4 HCAPLUS

CN Piperidine, 1-(cyclopropylacetyl)-4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]- (9CI) (CA INDEX NAME)



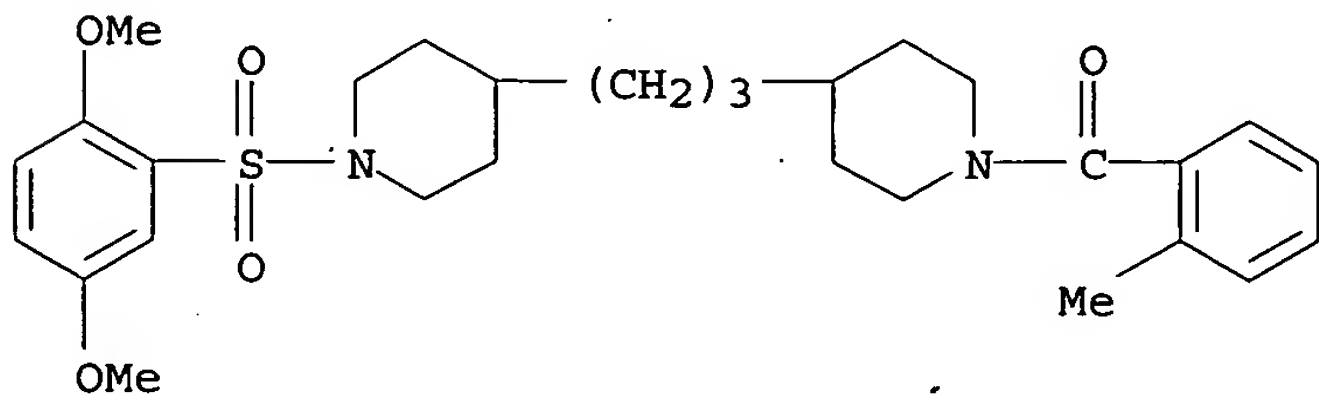
RN 479620-20-7 HCAPLUS

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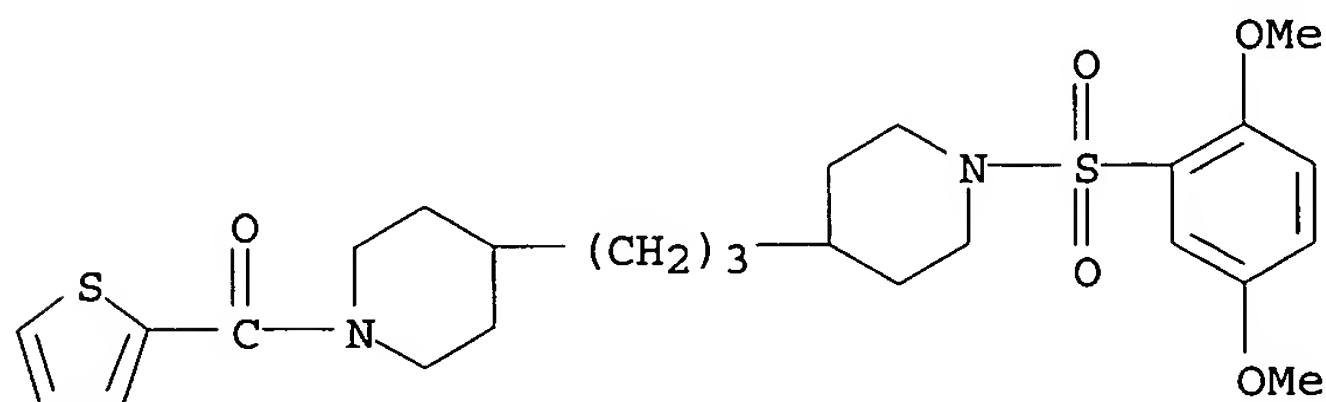
RN 479620-21-8 HCAPLUS

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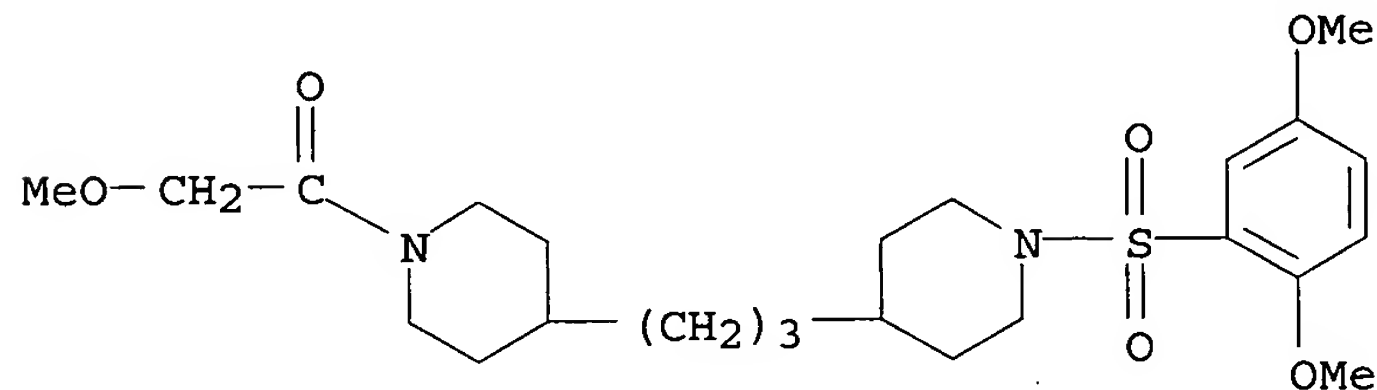
RN 479620-22-9 HCAPLUS

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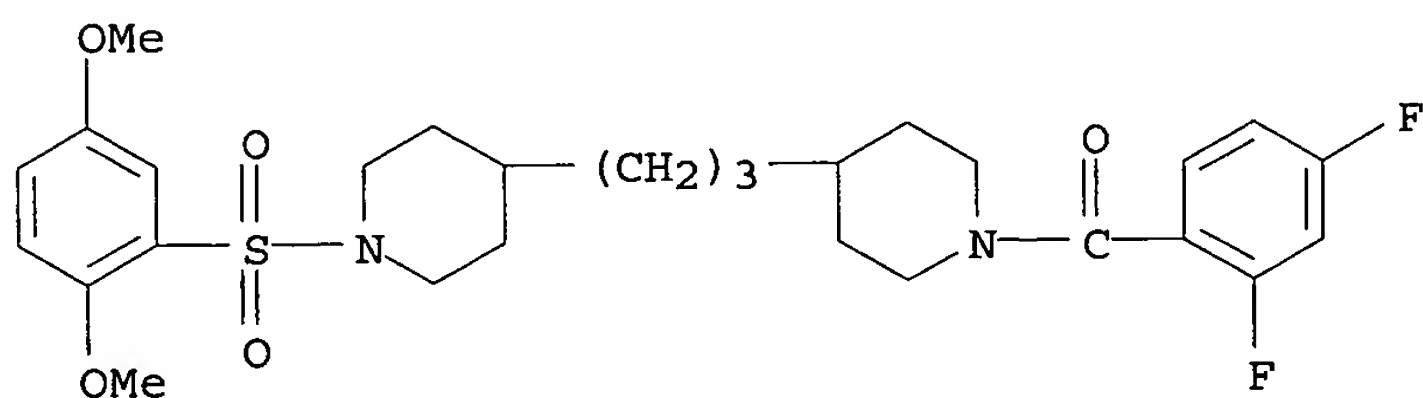
RN 479620-23-0 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-(methoxyacetyl)- (9CI) (CA INDEX NAME)



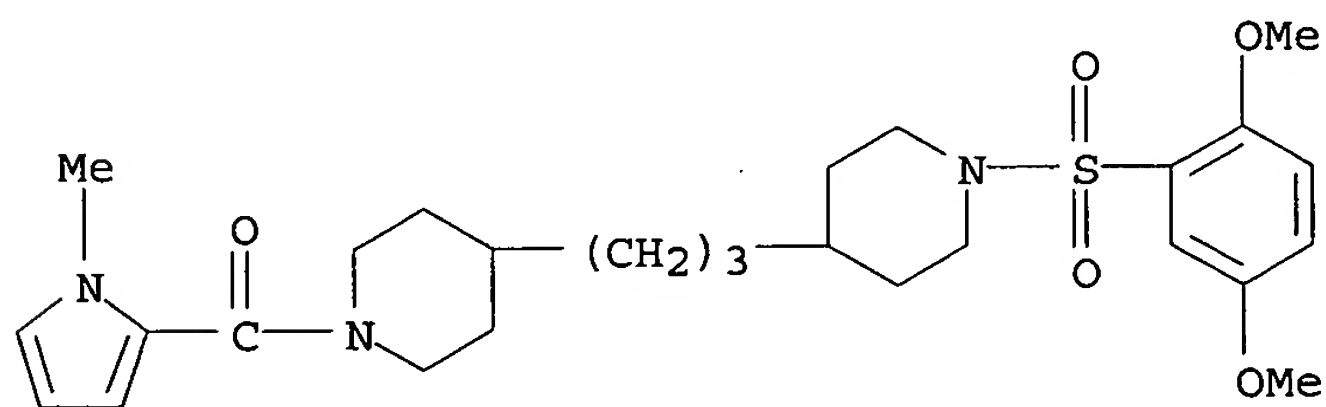
RN 479620-24-1 HCAPLUS

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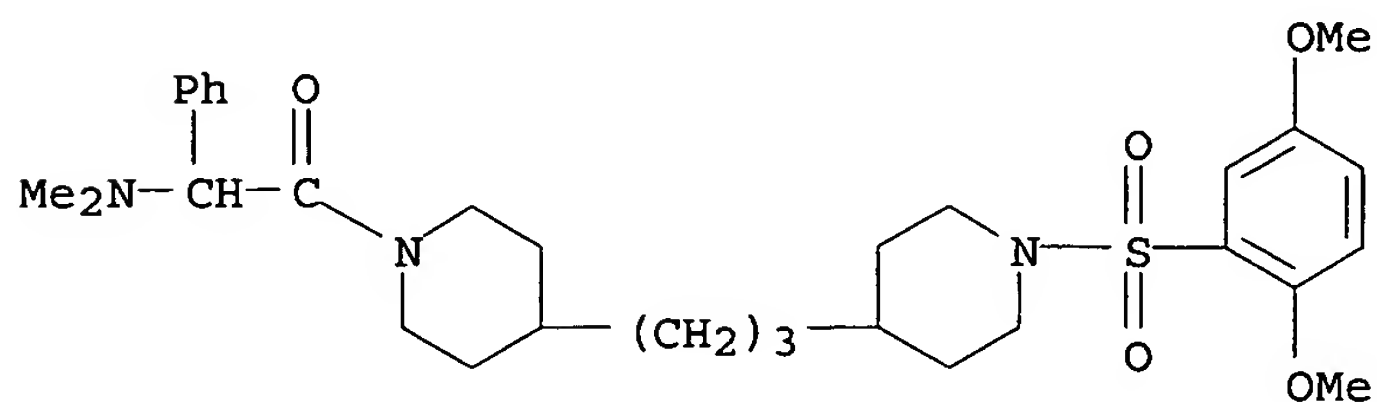
RN 479620-25-2 HCAPLUS

CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-[(1-methyl-1H-pyrrol-2-yl)carbonyl]- (9CI) (CA INDEX NAME)



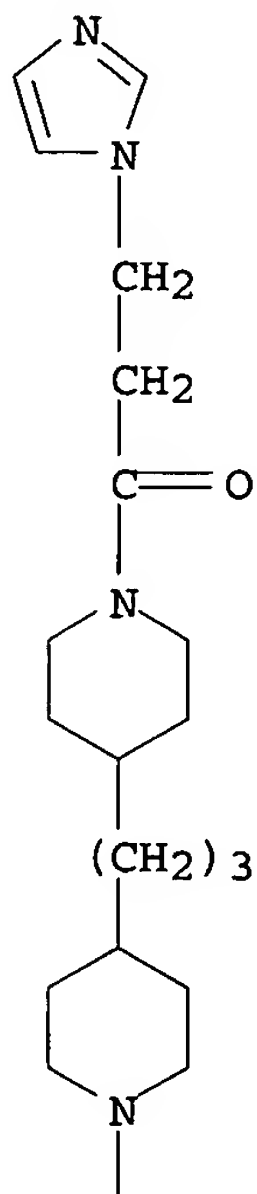


RN 479620-26-3 HCAPLUS  
 CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-  
 1-[(dimethylamino)phenylacetyl]- (9CI) (CA INDEX NAME)

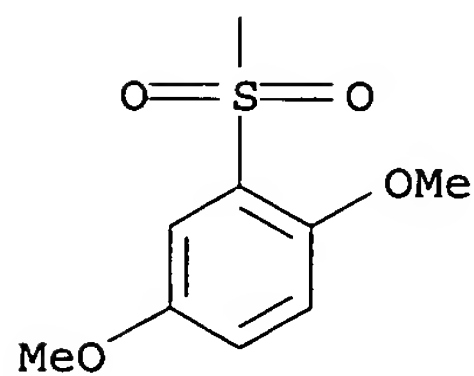


RN 479620-27-4 HCAPLUS  
 CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-  
 1-[3-(1H-imidazol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

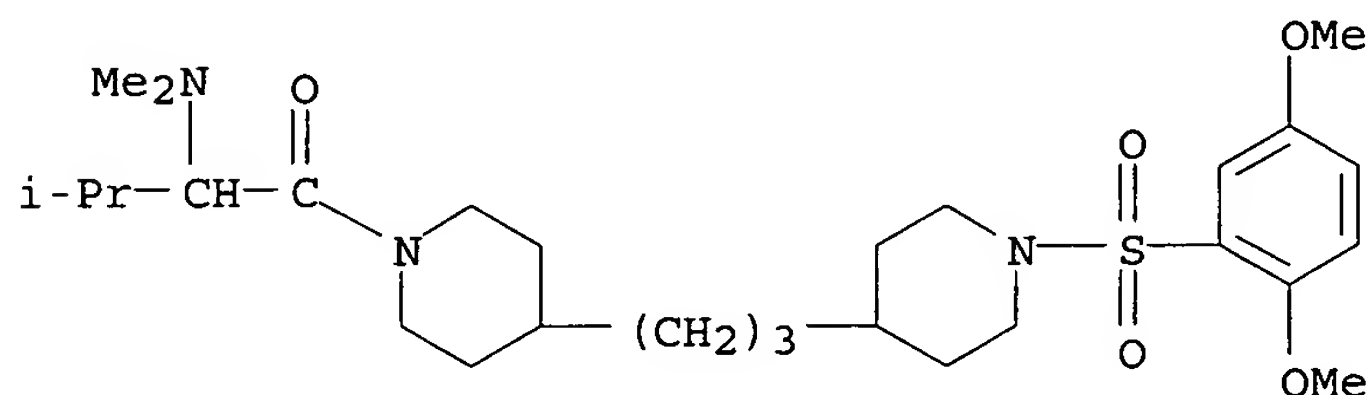
PAGE 1-A



PAGE 2-A



RN 479620-28-5 HCAPLUS  
 CN Piperidine, 4-[3-[1-[(2,5-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-1-[2-(dimethylamino)-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

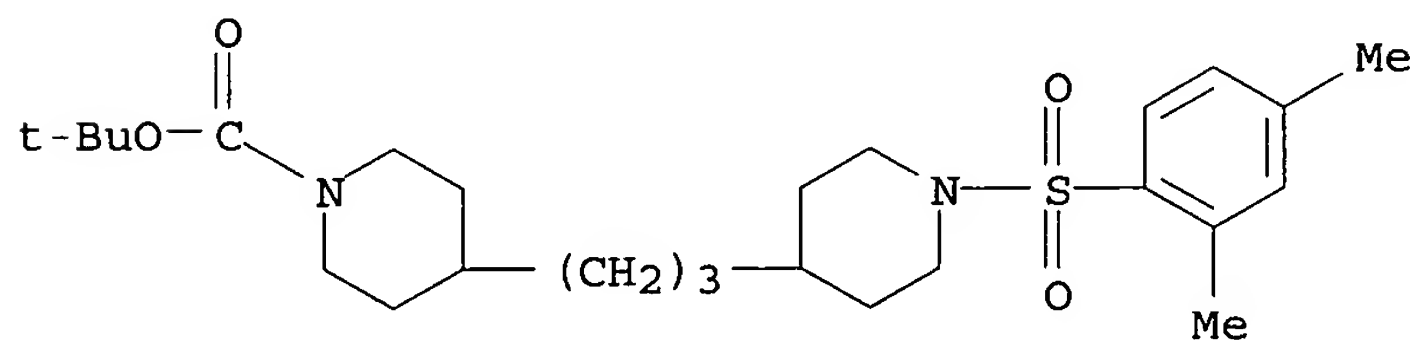


IT 479618-33-2P 479618-34-3P 479618-35-4P  
 479618-36-5P 479618-37-6P 479618-38-7P  
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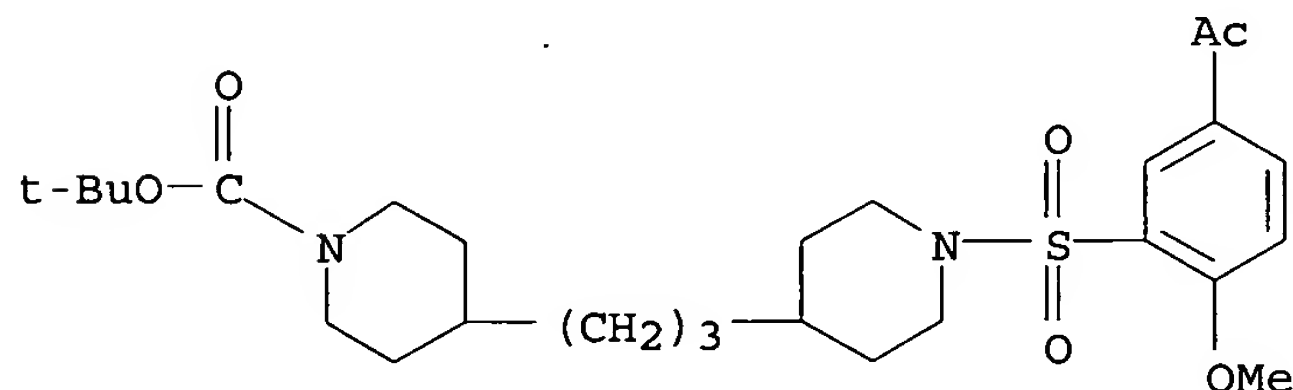
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of bispiperidines as antibacterial agents and inhibitors of phosphopantetheine adenylyl transferase)

RN 479618-33-2 HCAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2,4-dimethylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

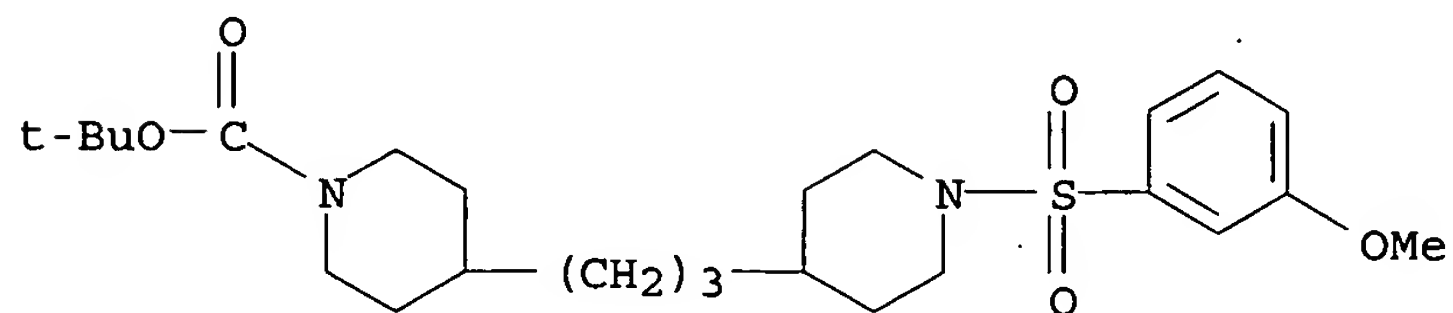


RN 479618-34-3 HCAPLUS  
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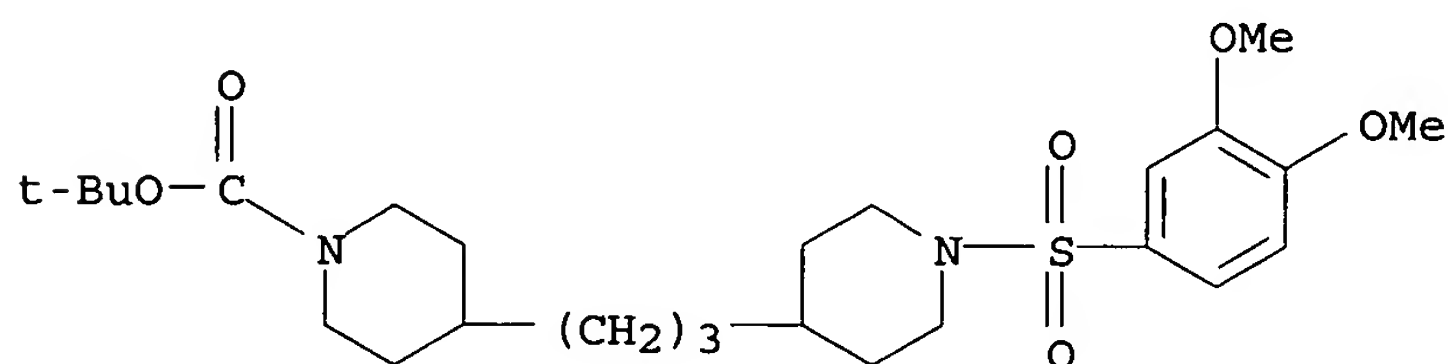
RN 479618-35-4 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3-methoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



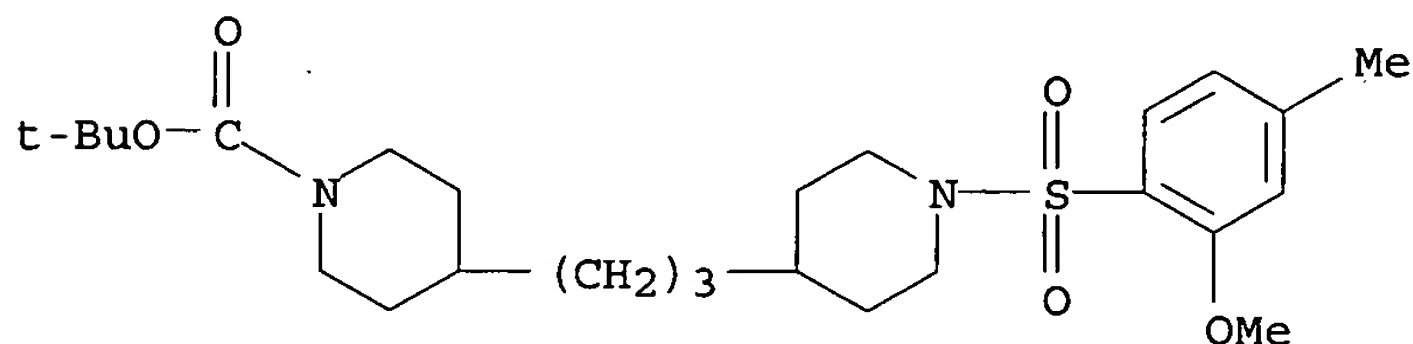
RN 479618-36-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3,4-dimethoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



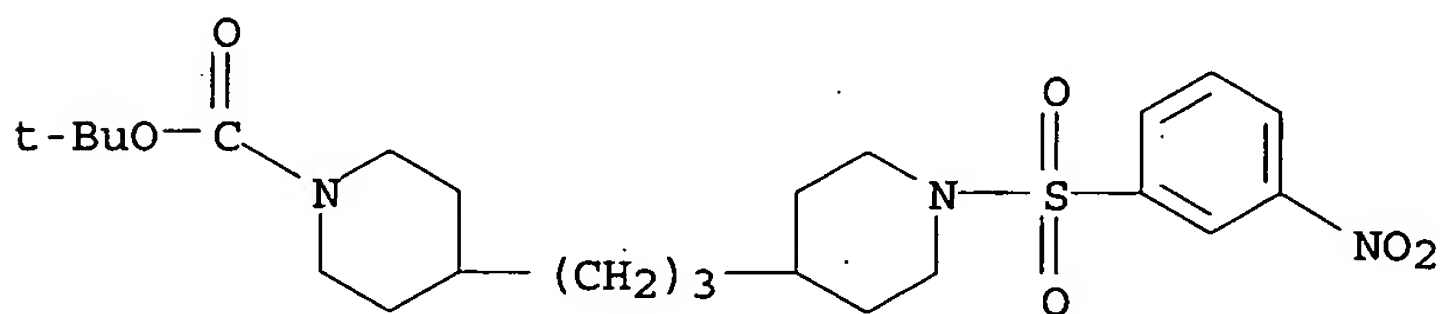
RN 479618-37-6 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-methoxy-4-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



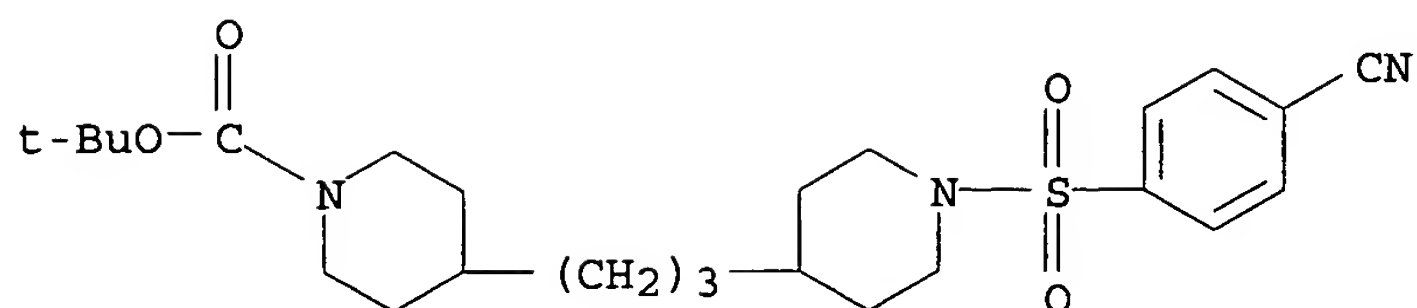
RN 479618-38-7 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3-nitrophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



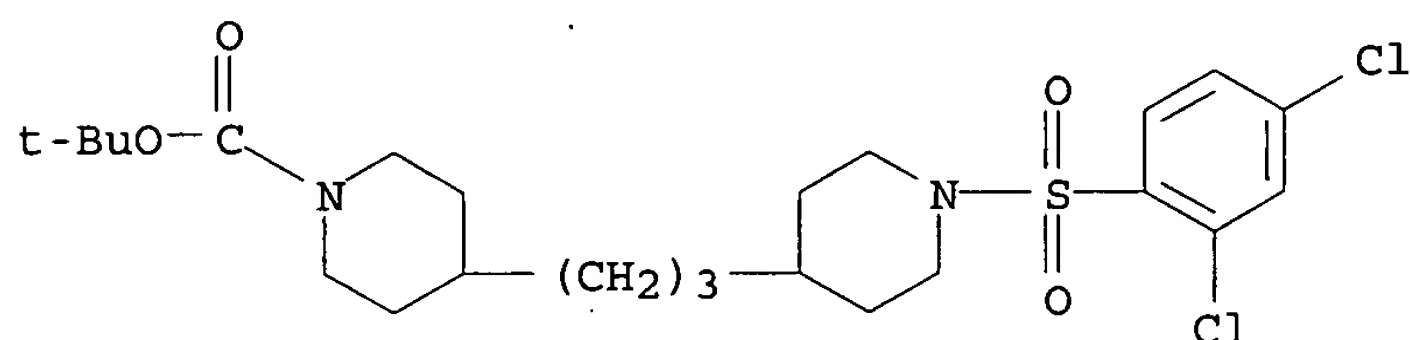
RN 479618-39-8 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(4-cyanophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



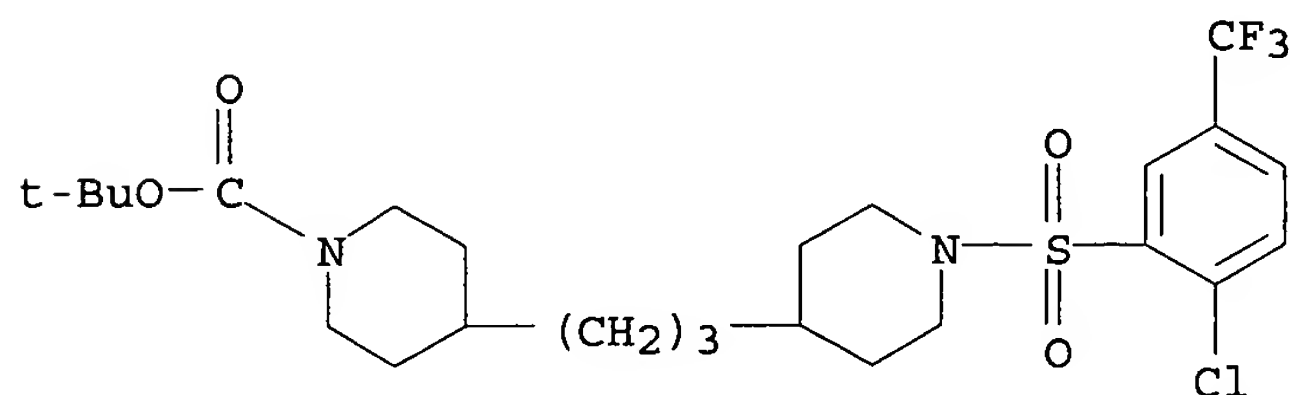
RN 479618-40-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2,4-dichlorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



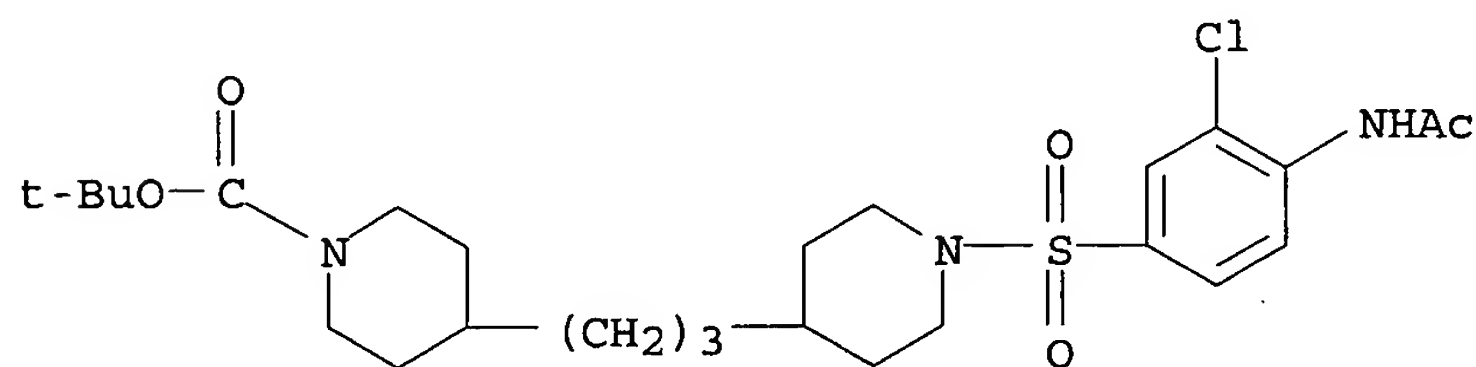
RN 479618-41-2 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



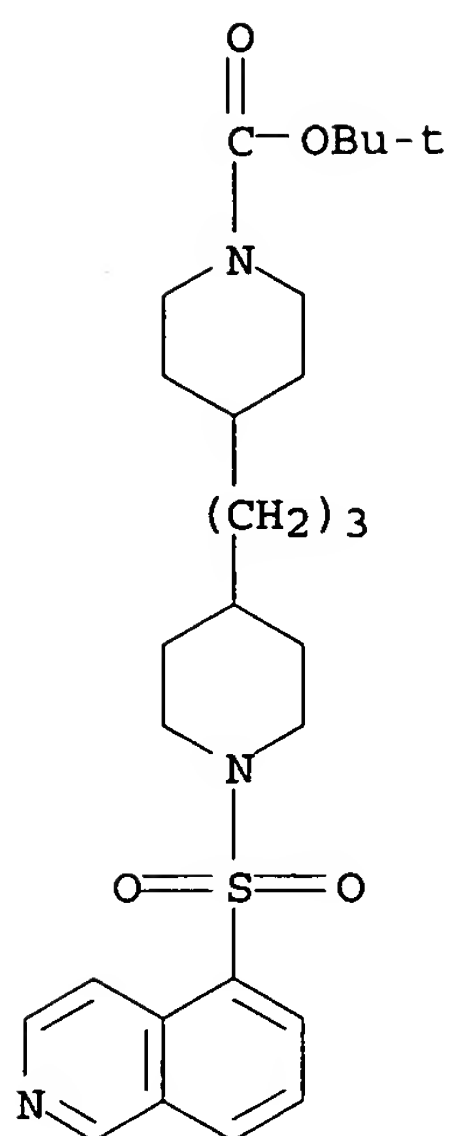
RN 479618-42-3 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[4-(acetylamino)-3-chlorophenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



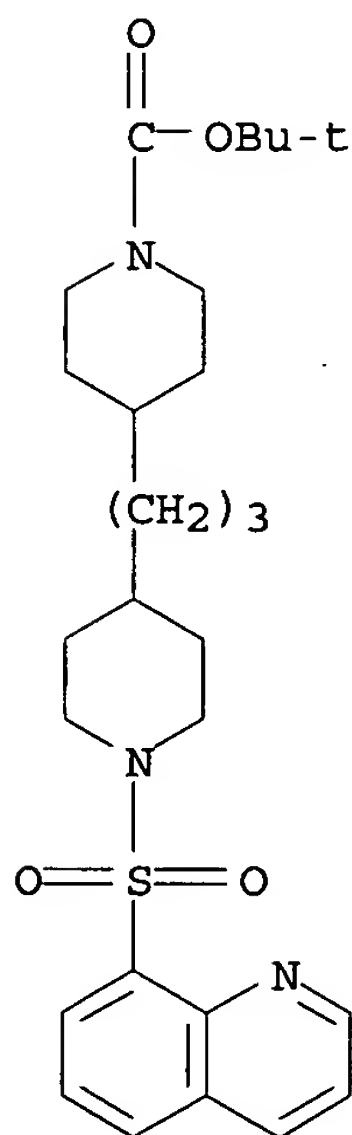
RN 479618-43-4 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-(5-isoquinoliny)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



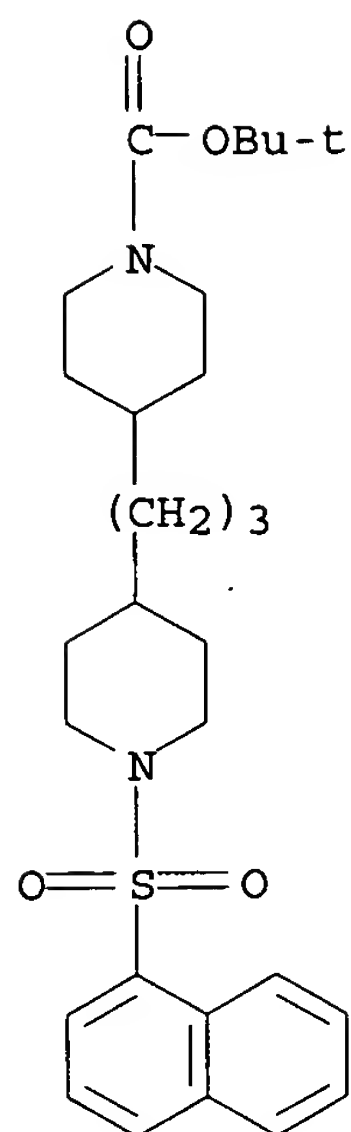
RN 479618-44-5 HCAPLUS

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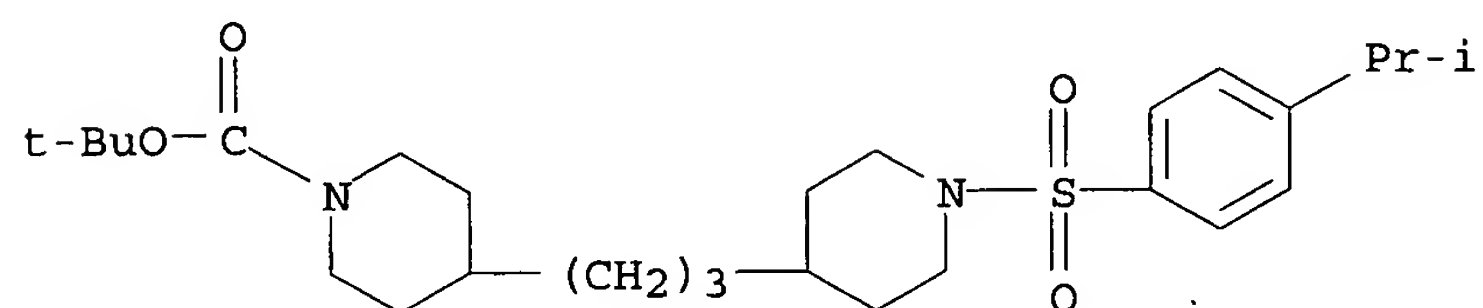


RN 479618-45-6 HCAPLUS

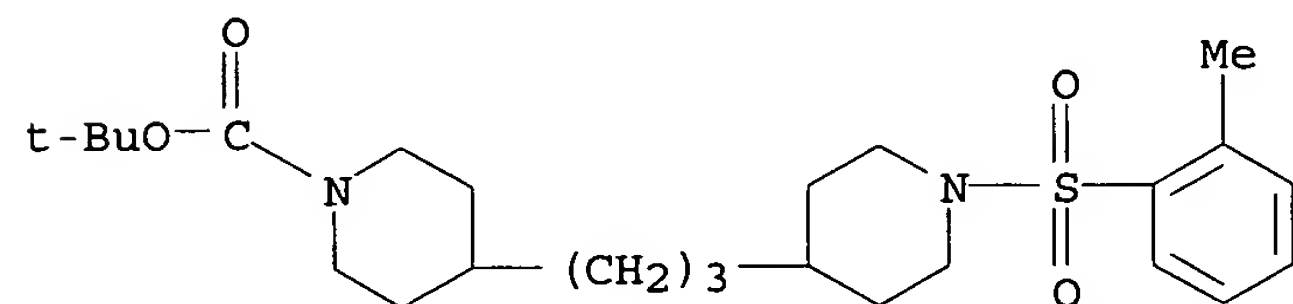
CN 1-Piperidinecarboxylic acid, 4-[3-[1-(1-naphthalenylsulfonyl)-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



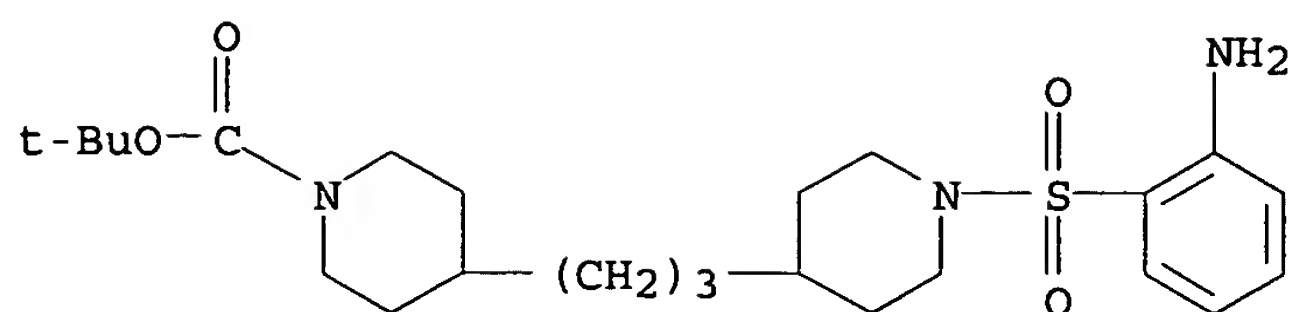
RN 479618-46-7 HCAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[4-(1-methylethyl)phenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 479618-47-8 HCAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

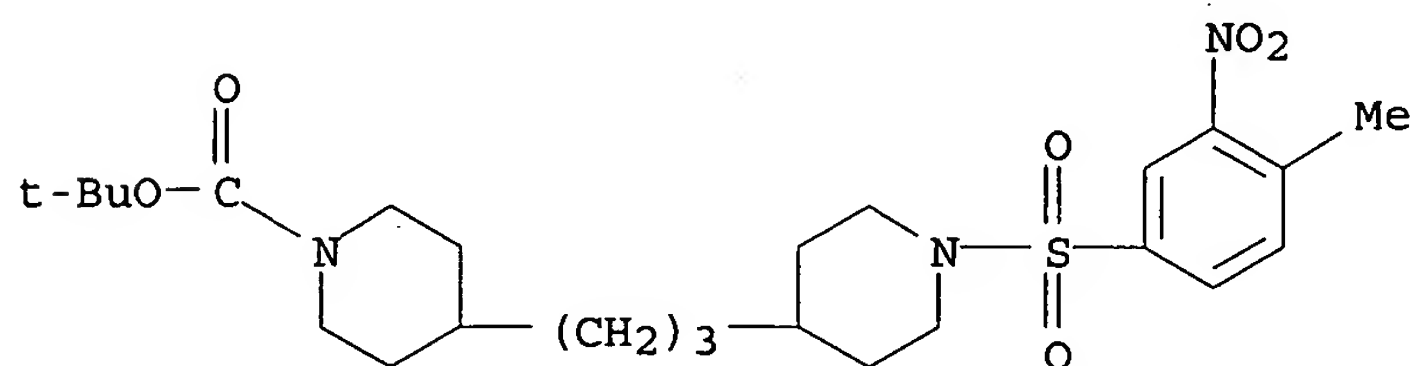


RN 479618-48-9 HCAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-aminophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



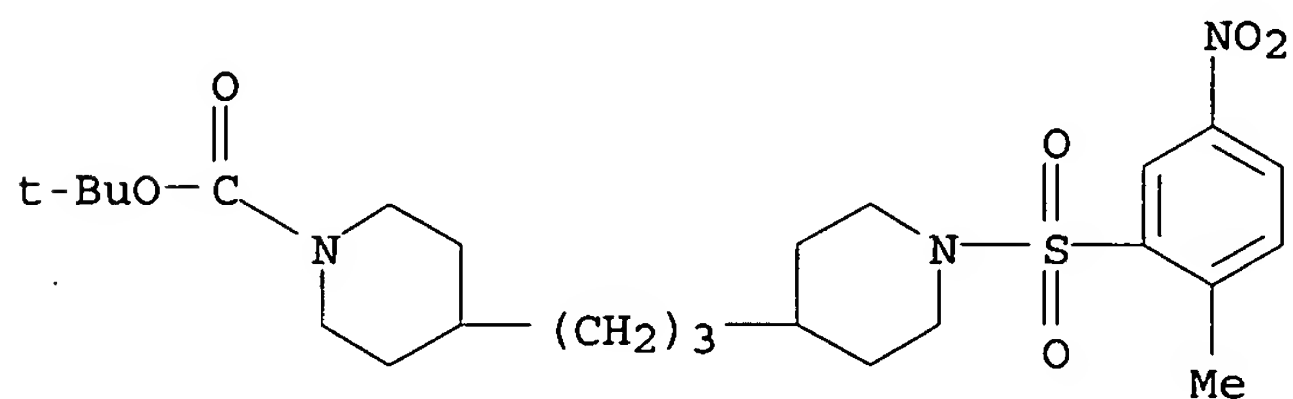
RN 479618-49-0 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(4-amino-3-nitrophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



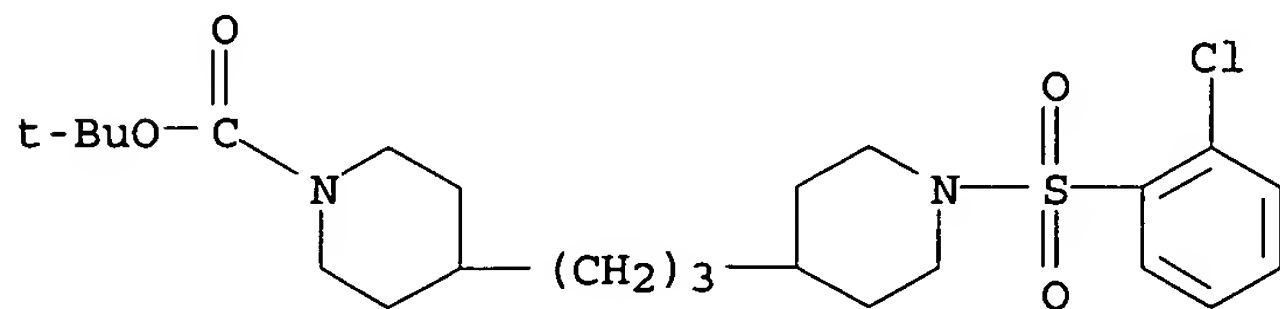
RN 479618-50-3 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-methyl-5-nitrophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



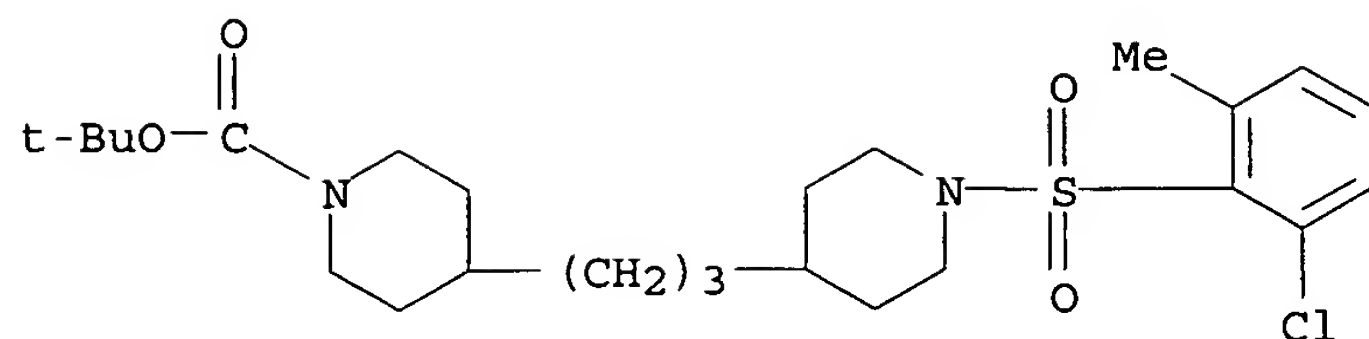
RN 479618-51-4 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-chlorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

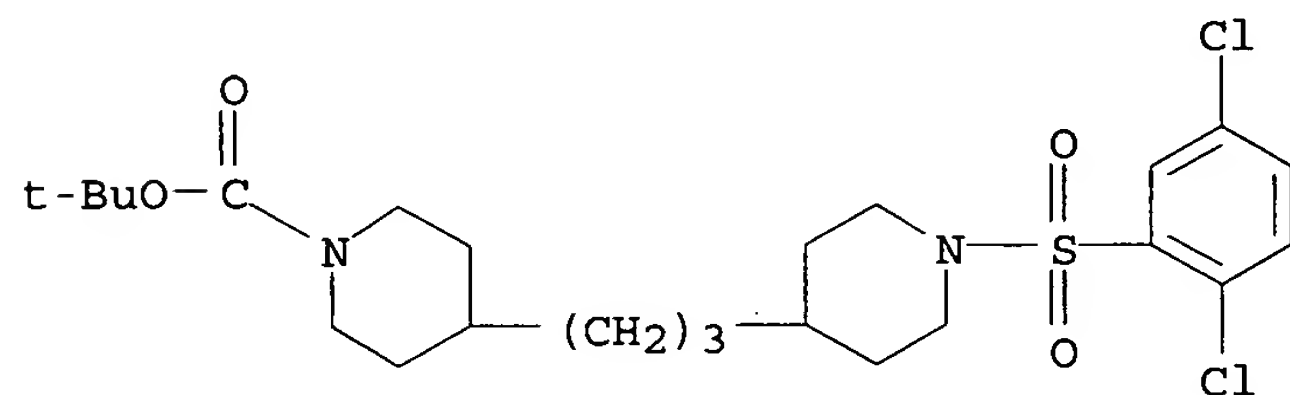


RN 479618-52-5 HCAPLUS

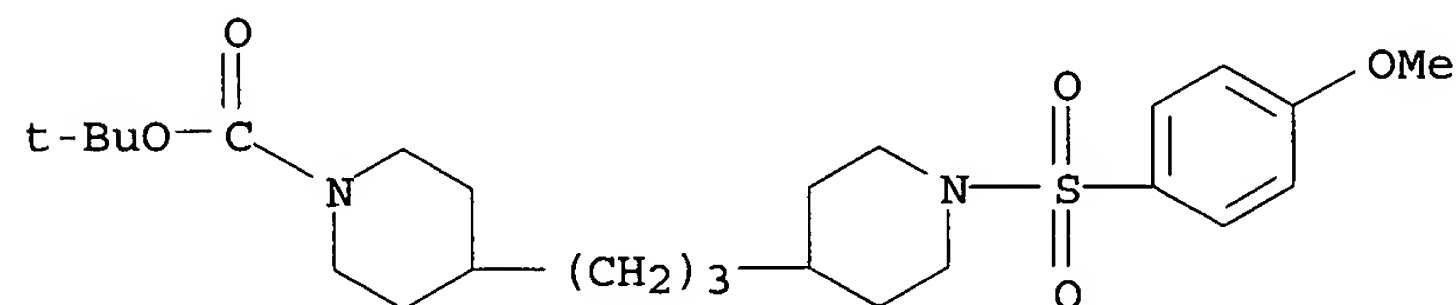
CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-chloro-6-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



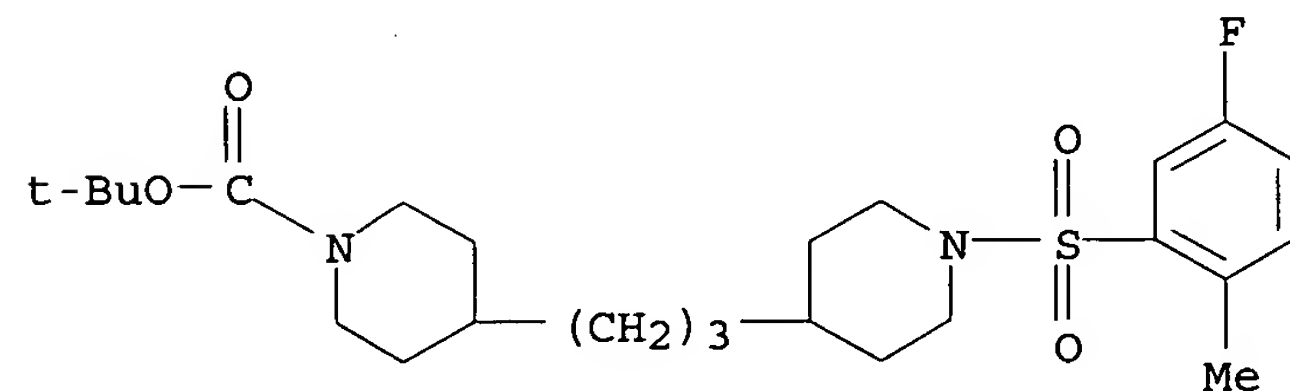
RN 479618-53-6 HCAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2,5-dichlorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 479618-54-7 HCAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

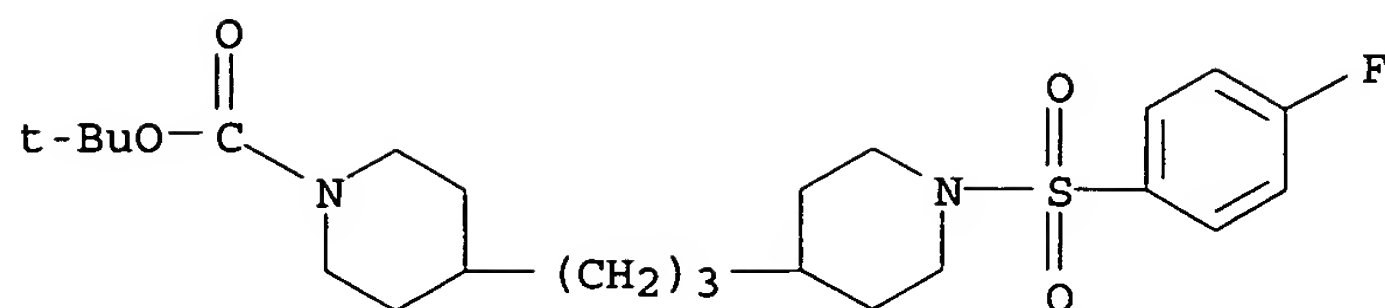


RN 479618-55-8 HCAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(5-fluoro-2-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



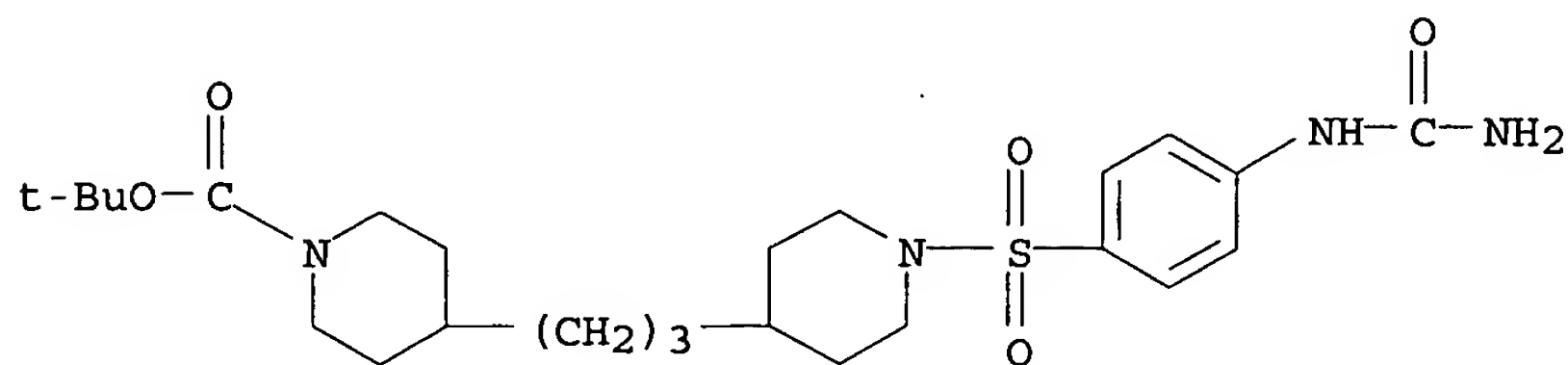
RN 479618-56-9 HCAPLUS  
 CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(4-fluorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)





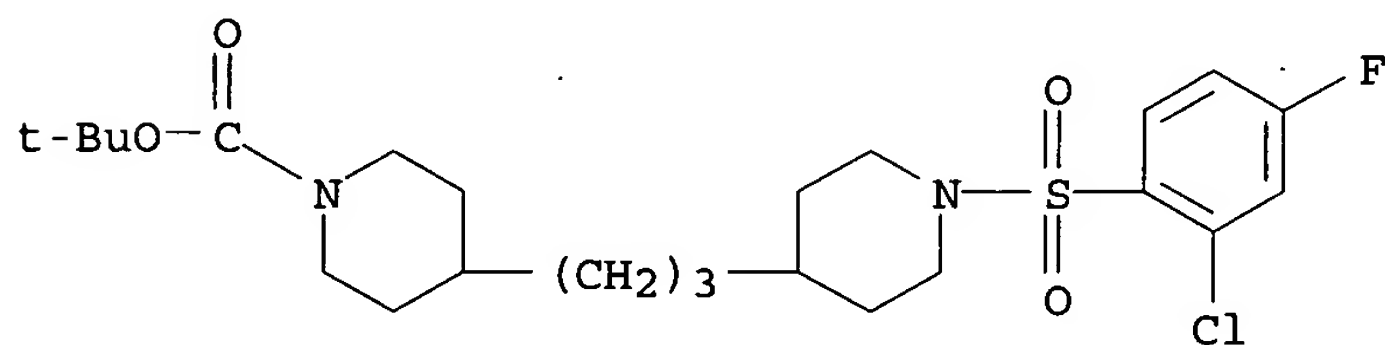
RN 479618-57-0 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[4-[(aminocarbonyl)amino]phenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



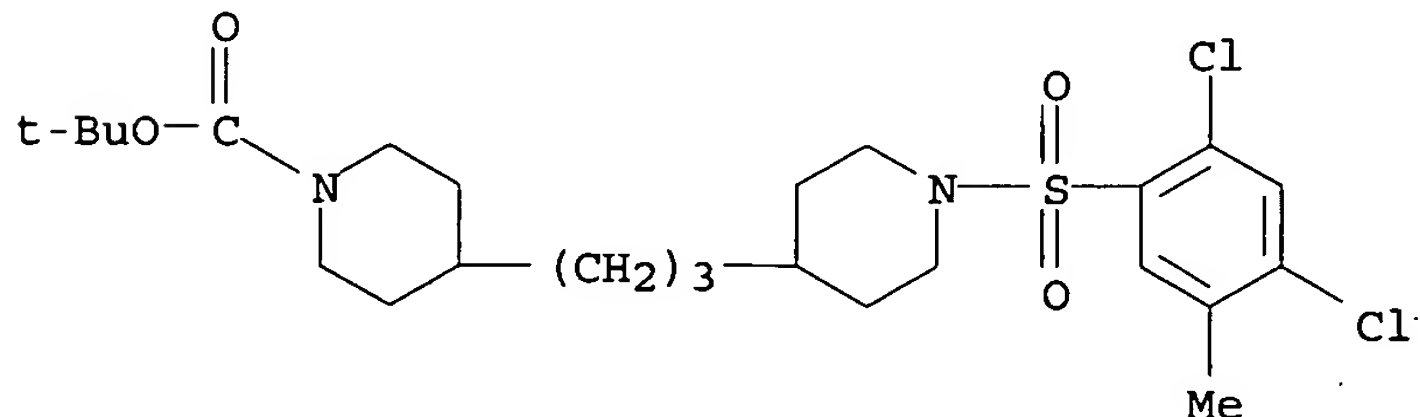
RN 479618-58-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2-chloro-4-fluorophenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



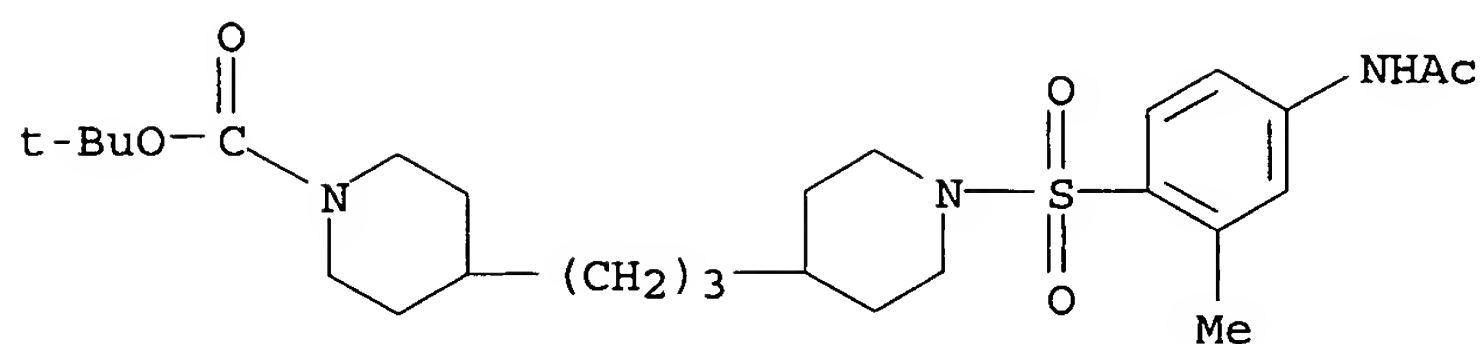
RN 479618-59-2 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(2,4-dichloro-5-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



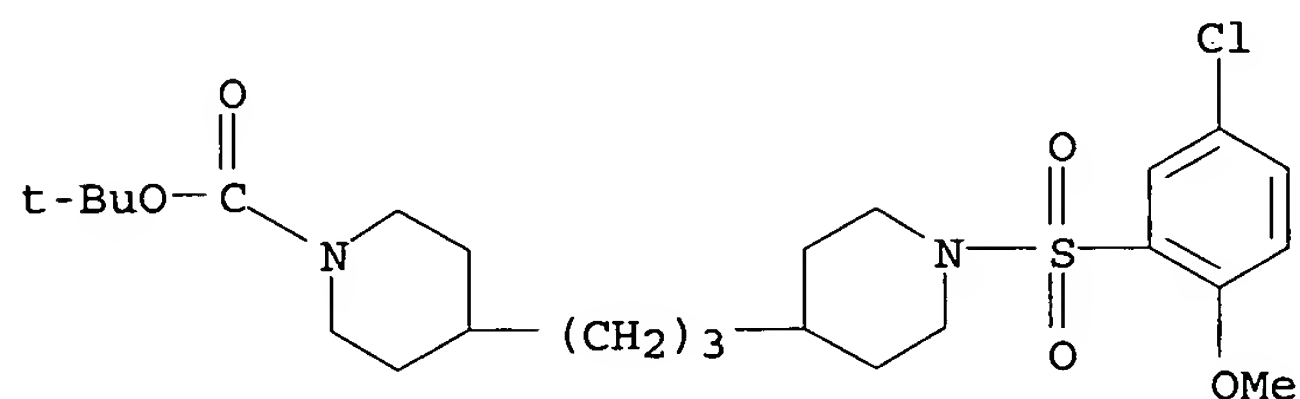
RN 479618-60-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[4-(acetylamino)-2-methylphenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



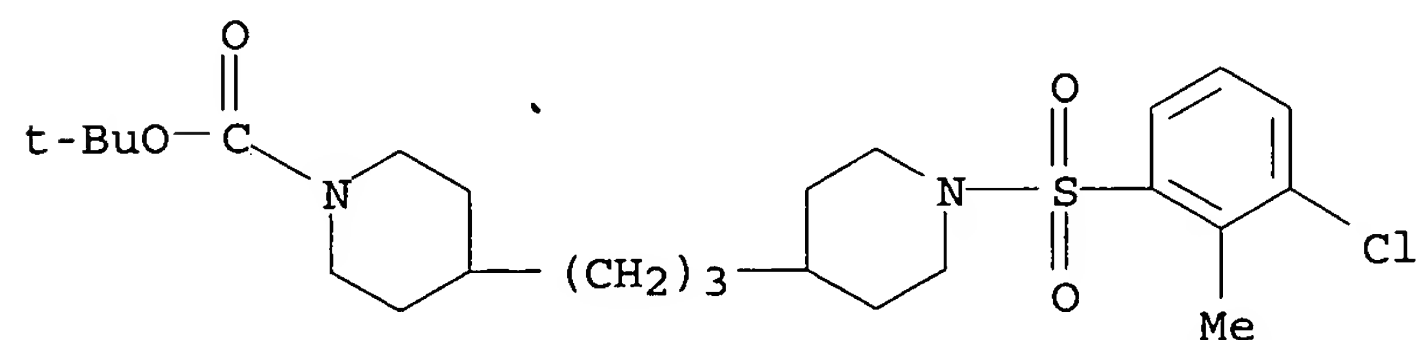
RN 479618-61-6 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(5-chloro-2-methoxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



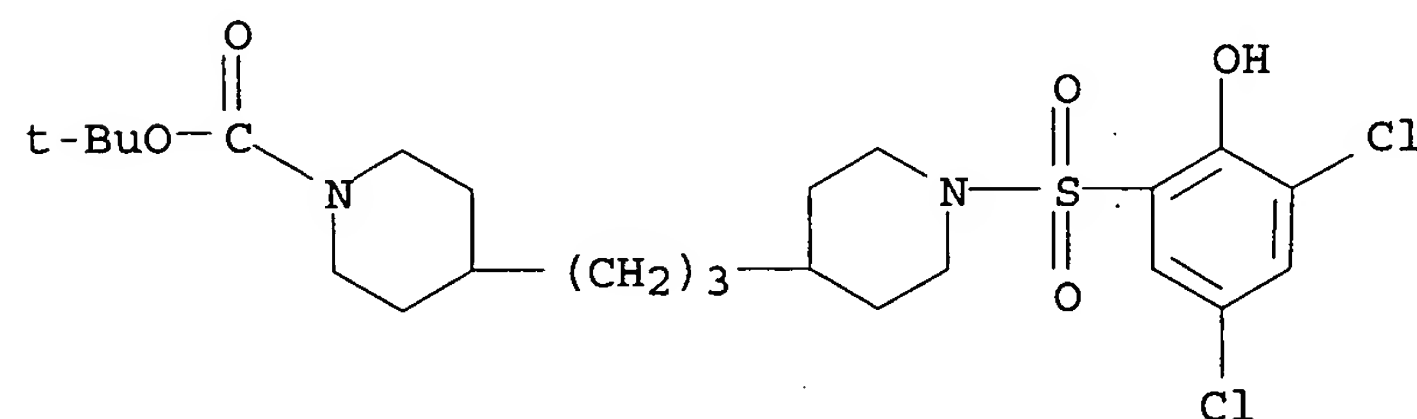
RN 479618-62-7 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3-chloro-2-methylphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



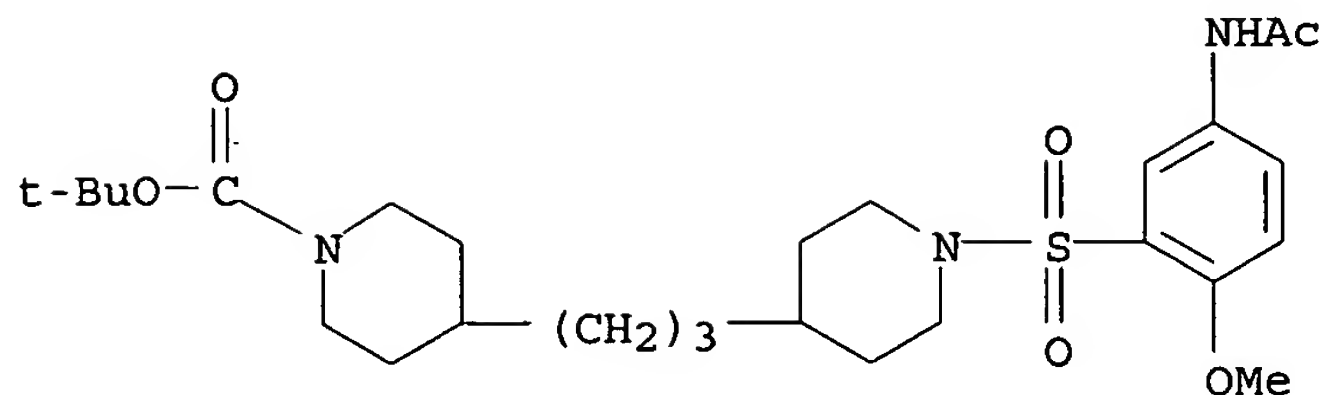
RN 479618-63-8 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[(3,5-dichloro-2-hydroxyphenyl)sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 479618-64-9 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[1-[[5-(acetylamino)-2-methoxyphenyl]sulfonyl]-4-piperidinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:754206 HCAPLUS  
 DOCUMENT NUMBER: 137:273215  
 TITLE: Dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes  
 INVENTOR(S): Ashton, Wallace T.; Caldwell, Charles G.; Ok, Hyun; Parmee, Emma R.; Weber, Ann E.  
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA  
 SOURCE: PCT Int. Appl., 94 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076450	A1	20021003	WO 2002-US8931	20020322 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2441092	AA	20021003	CA 2002-2441092	20020322 <--
EP 1385508	A1	20040204	EP 2002-753819	20020322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004525929	T2	20040826	JP 2002-574965	20020322
US 2004106656	A1	20040603	US 2003-472771	20030924
PRIORITY APPLN. INFO.:			US 2001-278931P	P 20010327
			WO 2002-US8931	W 20020322

AB The present invention is directed to compds. which are inhibitors of the dipeptidyl peptidase-IV enzyme ("DP-IV inhibitors") and which are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which the dipeptidyl peptidase-IV enzyme is involved.

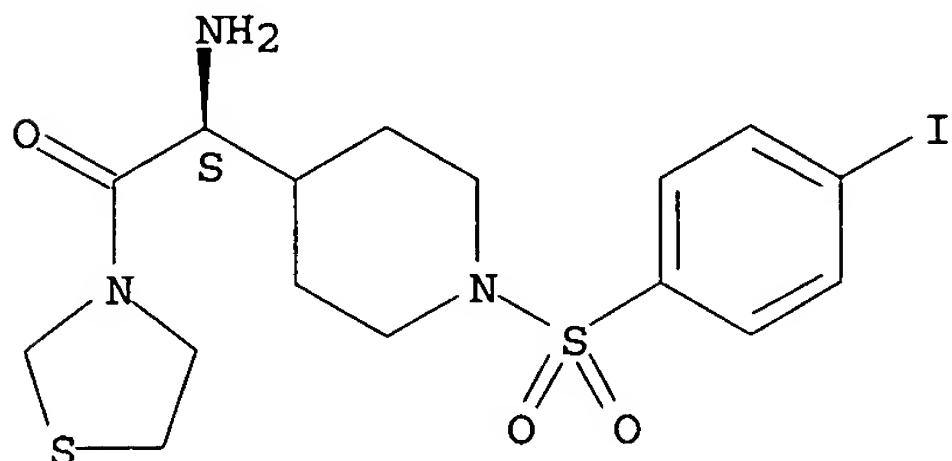
IT 463349-52-2P 463349-54-4P 463349-58-8P  
 463349-59-9P 463349-71-5P  
 RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes)

RN 463349-52-2 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-[(4-iodophenyl)sulfonyl]-4-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

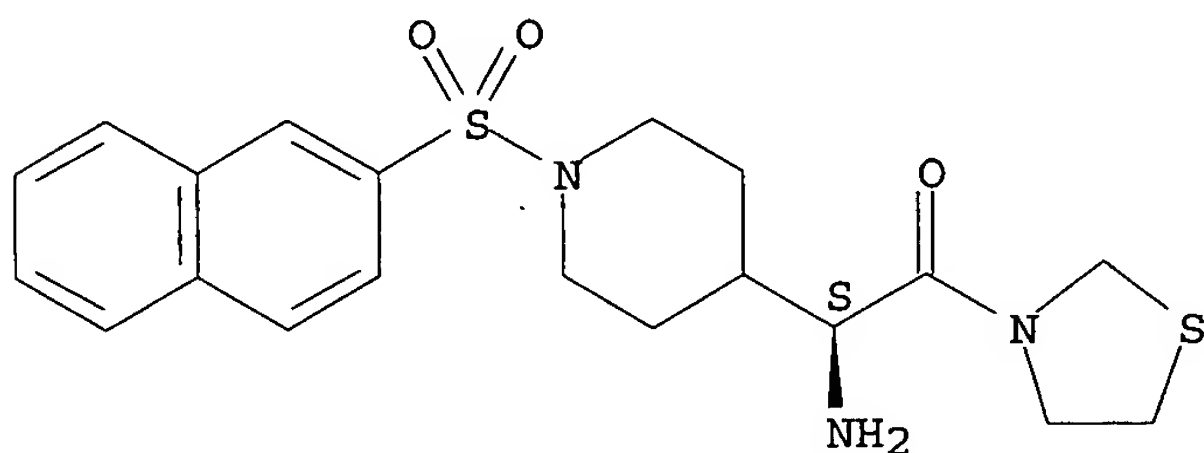
Absolute stereochemistry.



RN 463349-54-4 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-(2-naphthalenylsulfonyl)-4-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

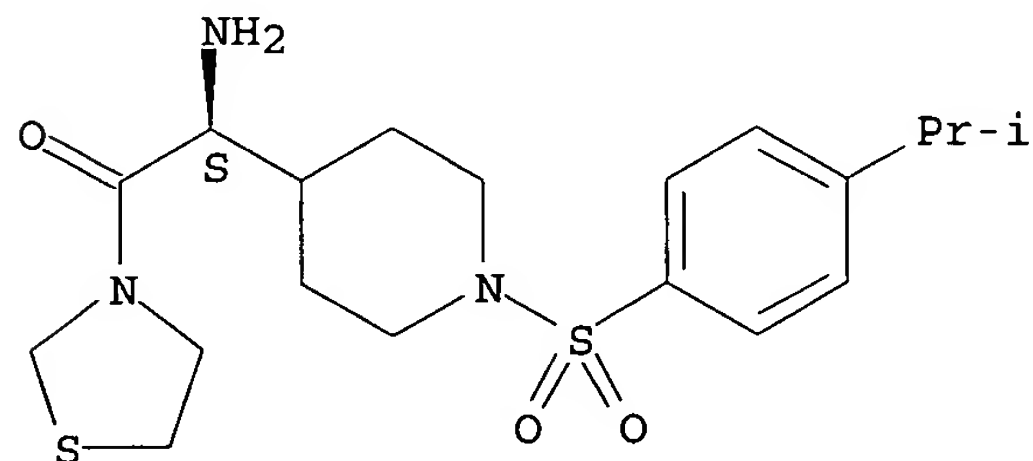
Absolute stereochemistry.



RN 463349-58-8 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-[[4-(1-methylethyl)phenyl]sulfonyl]-4-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

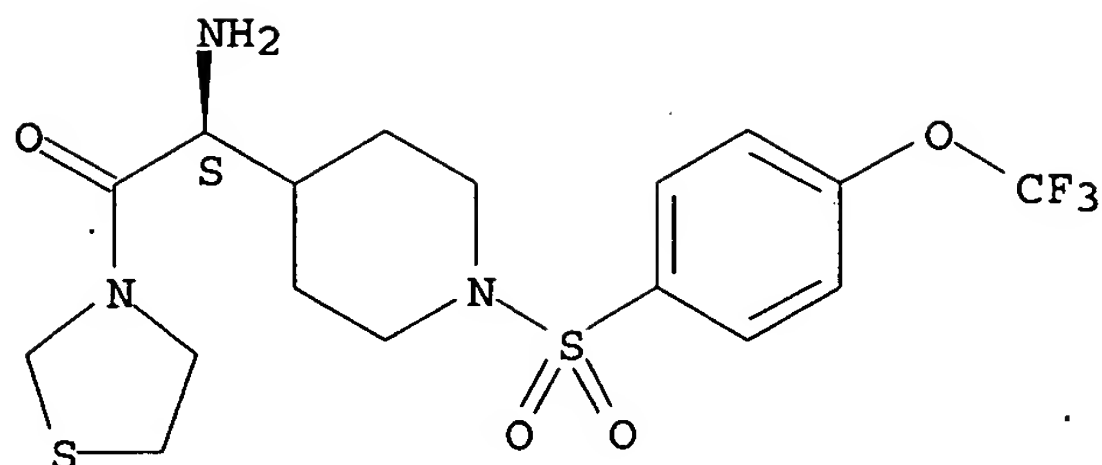
Absolute stereochemistry.



RN 463349-59-9 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-[[4-(trifluoromethoxy)phenyl]sulfonyl]-4-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

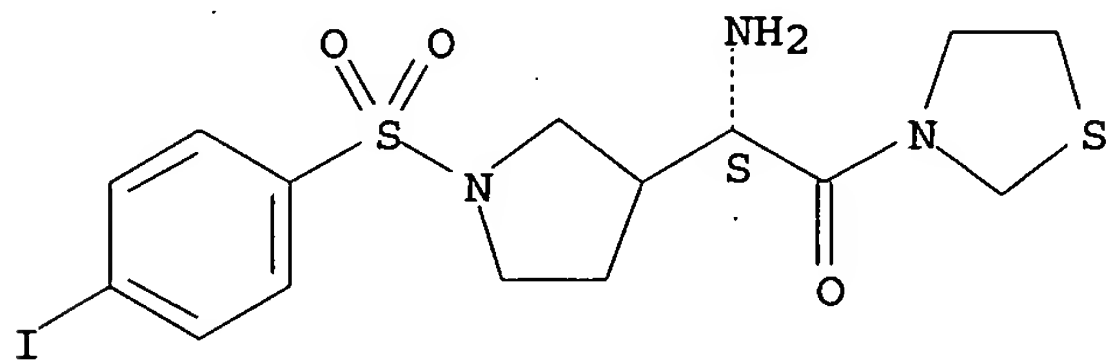
Absolute stereochemistry.



RN 463349-71-5 HCAPLUS

CN Thiazolidine, 3-[(2S)-amino[1-[(4-iodophenyl)sulfonyl]-3-pyrrolidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:637683 HCAPLUS

DOCUMENT NUMBER: 137:185504

TITLE: Preparation of thieno[2,3-d]pyrimidindiones as matrix metalloproteinase inhibitors for treatment of cancer, rheumatoid arthritis, and osteoarthritis

INVENTOR(S): Harter, William Glen; Li, Jie Jack; Ortwine, Daniel Fred; Shuler, Kevon Ray; Yue, Wen-song

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 278 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

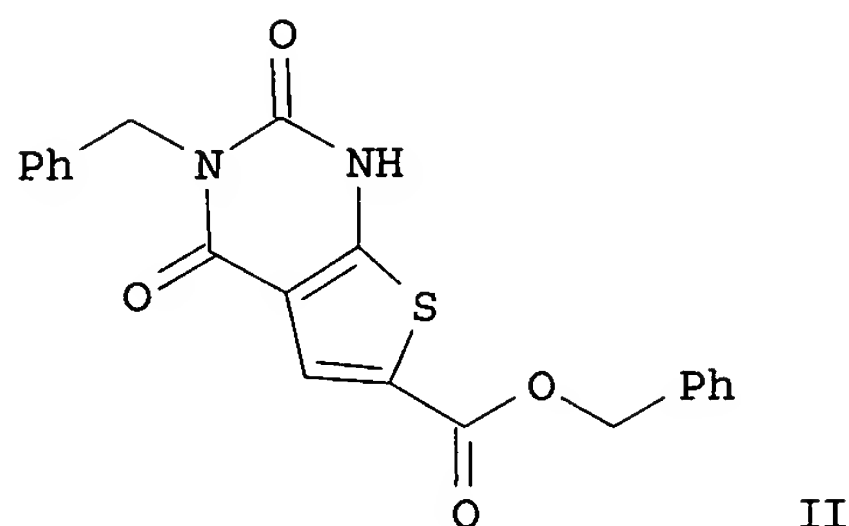
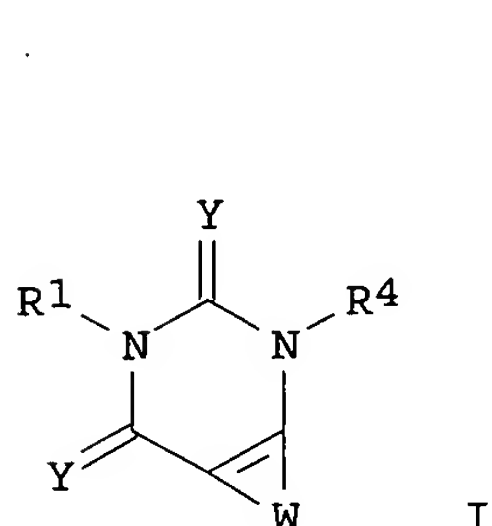
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064598	A1	20020822	WO 2002-IB204	20020118 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2433778	AA	20020822	CA 2002-2433778	20020118 <--

EP 1370562 A1 20031217 EP 2002-711123 20020118  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 BR 2002007216 A 20040309 BR 2002-7216 20020118  
 JP 2004518732 T2 20040624 JP 2002-564529 20020118  
 US 2003004172 A1 20030102 US 2002-75073 20020213 <--  
 PRIORITY APPLN. INFO.: US 2001-268756P P 20010214  
 WO 2002-IB204 W 20020118  
 OTHER SOURCE(S): MARPAT 137:185504  
 GI



AB Title fused pyrimidinones I [wherein C2W = 5-membered (hetero)cyclic diradical substituted with ABR3 and optionally substituted with R2; A = CO or SOO-2; B = O or NR5; or AB = C.tplbond.C; R1, R4, and R5 = independently H, alkyl, alkenyl, alkynyl, (CH2)n-(hetero)aryl, (CH2)n-cycloalkyl, (CH2)n-heterocyclyl, or alkanoyl; R2 and R3 = independently H, alkyl, alkenyl, alkynyl CN, NO2, NR4R5, (CH2)n-cycloalkyl, or (CH2)n-(hetero)aryl; or R2 = halo; n = 0-5; or NR4R5 = (un)substituted heterocyclyl; with the proviso that R1 and R3 ≠ both H or alkyl; or pharmaceutically acceptable salts thereof] were prepared as matrix metalloproteinase (MMP) **inhibitors**, especially as selective MMP-13 **inhibitors**. For example, 3-benzyl-6-chloro-1H-pyrimidine-2,4-dione was coupled with mercaptoacetic acid Et ester using Na2CO3 in EtOH (67%) and the product cyclized with POCl3 in anhydrous DMF to give 3-benzyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidine-6-carboxylic acid Et ester (95%). Saponification (96%) followed by esterification with benzyl

alc. and 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide metho-p-toluenesulfonate afforded II (12%). The latter selectively **inhibited** the hydrolytic activity of MMP-13 (0.61 μM) over MMP-1 (100 μM), MMP-2 (100 μM), MMP-3 (18 μM), MMP-7 (100 μM), MMP-9 (100 μM), MMP-12 (100 μM), and MMP-14 (100 μM) with the indicated IC50 values. I are useful for the treatment of diseases mediated by the MMP-13 **enzyme**, such as cancer, rheumatoid arthritis, or osteoarthritis (no data). Formulations of I are also disclosed.

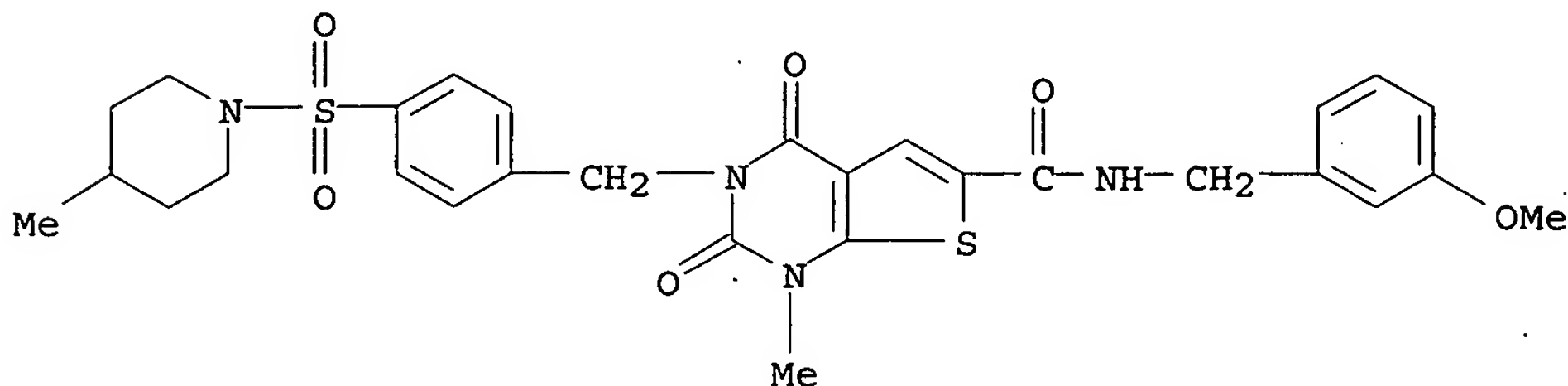
IT 448965-29-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(MMP **inhibitor**; preparation of thienopyrimidinediones as MMP **inhibitors** for treatment of cancer, rheumatoid arthritis, and osteoarthritis)

RN 448965-29-5 HCAPLUS

CN Thieno[2,3-d]pyrimidine-6-carboxamide, 1,2,3,4-tetrahydro-N-[(3-methoxyphenyl)methyl]-1-methyl-3-[[4-[(4-methyl-1-piperidinyl)sulfonyl]phenyl]methyl]-2,4-dioxo- (9CI) (CA INDEX NAME)



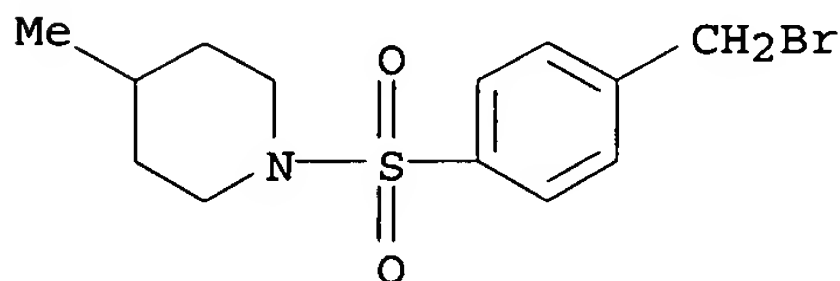
IT 448965-30-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; preparation of thienopyrimidinediones as MMP inhibitors for treatment of cancer, rheumatoid arthritis, and osteoarthritis)

RN 448965-30-8 HCAPLUS

CN Piperidine, 1-[[4-(bromomethyl)phenyl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:449662 HCAPLUS

DOCUMENT NUMBER: 137:33310

TITLE: Preparation of anilinopyrimidines as IKK inhibitors

INVENTOR(S): Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.

PATENT ASSIGNEE(S): Signal Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 194 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

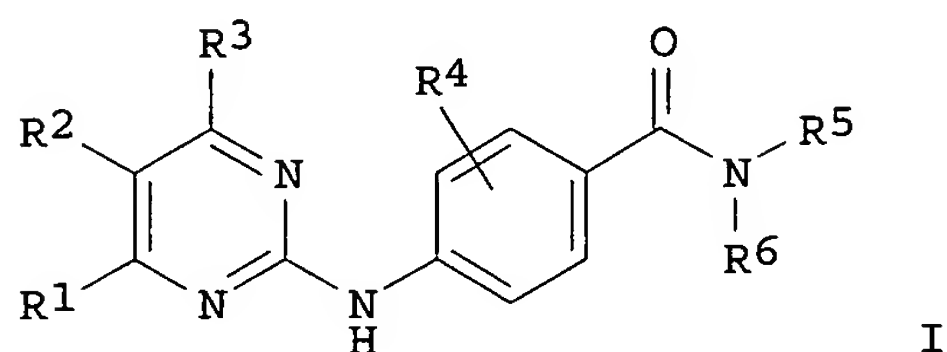
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046171	A2	20020613	WO 2001-US46403	20011205 <--
WO 2002046171	A3	20030123		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,

UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 US 2003203926 A1 20031030 US 2001-4642 20011204 <--  
 CA 2431160 AA 20020613 CA 2001-2431160 20011205 <--  
 AU 2002020195 A5 20020618 AU 2002-20195 20011205 <--  
 EP 1349841 A2 20031008 EP 2001-999564 20011205 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2004523497 T2 20040805 JP 2002-547910 20011205  
 PRIORITY APPLN. INFO.: US 2000-251816P P 20001206  
 WO 2001-US46403 W 20011205  
 OTHER SOURCE(S): MARPAT 137:33310  
 GI



AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as **inhibitors** of IKK, particularly IKK-2, were prepared E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of  $\leq 1 \mu\text{M}$  in the IKK-2 **enzyme** assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to IKK **inhibition**. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. containing one or more compds. of the above compds.

IT 434949-91-4P 434949-95-8P 434949-96-9P  
 434949-97-0P

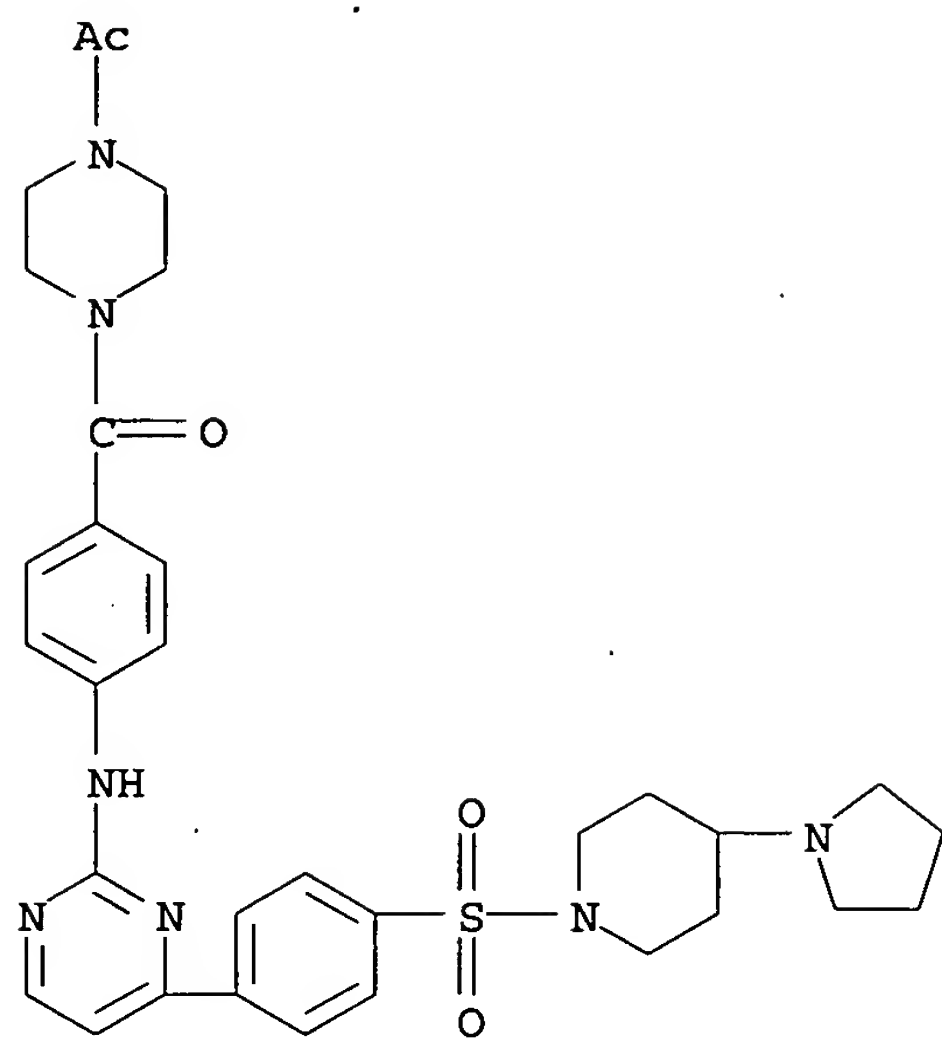
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of anilinopyrimidines as IKK **inhibitors**)

RN 434949-91-4 HCAPLUS

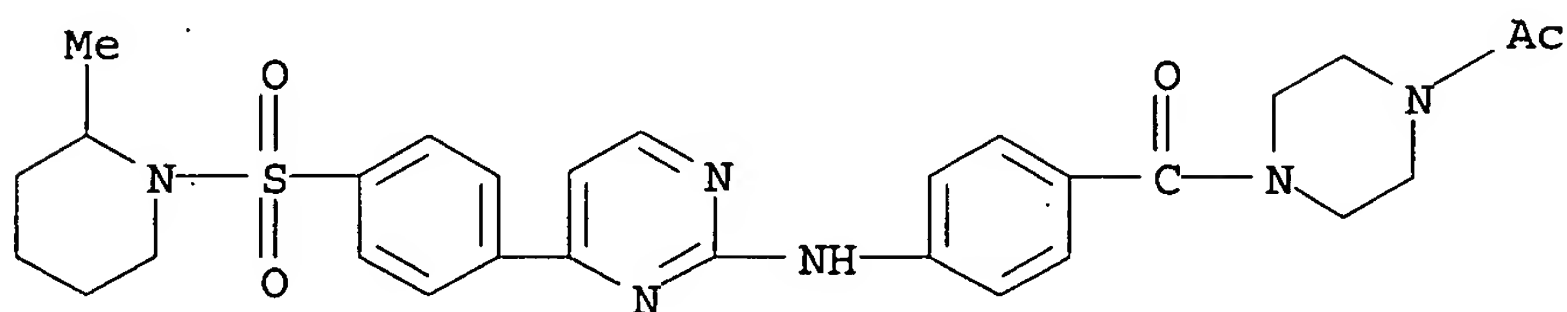
CN Piperazine, 1-acetyl-4-[4-[[4-[4-[[4-(1-pyrrolidinyl)-1-piperidinyl]sulfonyl]phenyl]-2-pyrimidinyl]amino]benzoyl]- (9CI) (CA INDEX NAME)





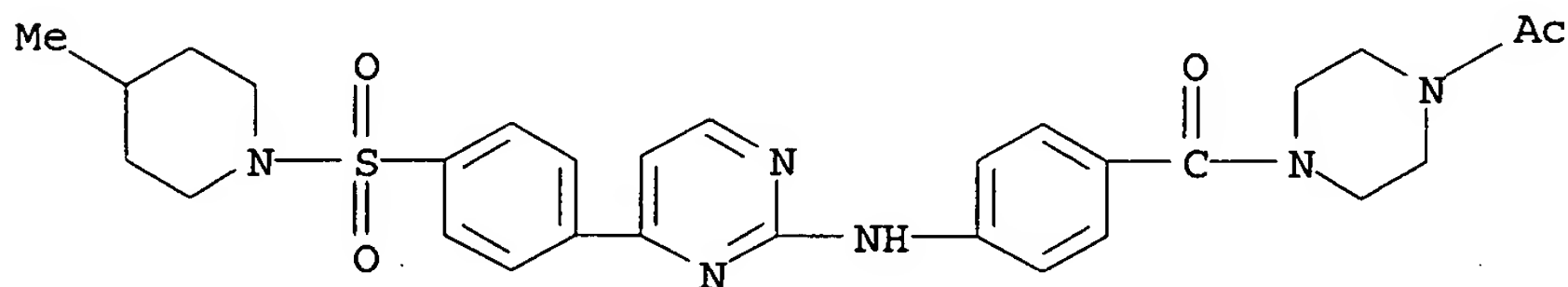
RN 434949-95-8 HCAPLUS

CN Piperazine, 1-acetyl-4-[4-[[4-[4-[(2-methyl-1-piperidinyl)sulfonyl]phenyl]-2-pyrimidinyl]amino]benzoyl]- (9CI) (CA INDEX NAME)



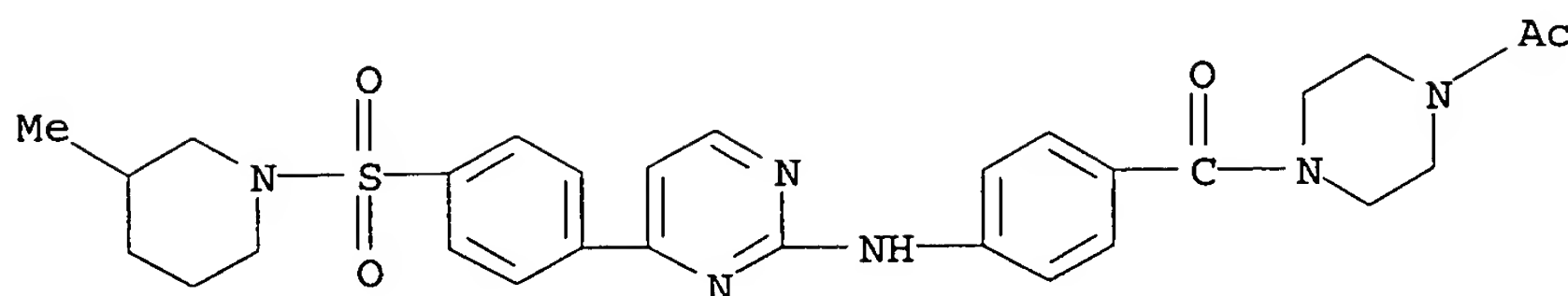
RN 434949-96-9 HCAPLUS

CN Piperazine, 1-acetyl-4-[4-[[4-[4-[(4-methyl-1-piperidinyl)sulfonyl]phenyl]-2-pyrimidinyl]amino]benzoyl]- (9CI) (CA INDEX NAME)



RN 434949-97-0 HCAPLUS

CN Piperazine, 1-acetyl-4-[4-[[4-[4-[(3-methyl-1-piperidinyl)sulfonyl]phenyl]-2-pyrimidinyl]amino]benzoyl]- (9CI) (CA INDEX NAME)



L32 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:314395 HCAPLUS  
 DOCUMENT NUMBER: 136:335540  
 TITLE: Use of PDE V inhibitors for improved fecundity in mammals  
 INVENTOR(S): Westbrook, Simon Lempriere; Zanzinger, Johannes Friedrich  
 PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.  
 SOURCE: Eur. Pat. Appl., 20 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1199070	A2	20020424	EP 2001-308684	20011011 <--
EP 1199070	A3	20040317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2359383	AA	20020420	CA 2001-2359383	20011018 <--
US 2003018036	A1	20030123	US 2001-982445	20011018 <--
US 6548508	B2	20030415		
JP 2002220346	A2	20020809	JP 2001-322195	20011019 <--
ZA 2001008617	A	20030422	ZA 2001-8617	20011019 <--
NZ 514947	A	20050324	NZ 2001-514947	20011019
US 2003018037	A1	20030123	US 2002-229534	20020827 <--
US 6743799	B2	20040601		
US 2004167095	A1	20040826	US 2004-778866	20040212
PRIORITY APPLN. INFO.:			GB 2000-25782	A 20001020
			US 2000-253338P	P 20001128
			US 2001-982445	A1 20011018
			US 2002-229534	A1 20020827

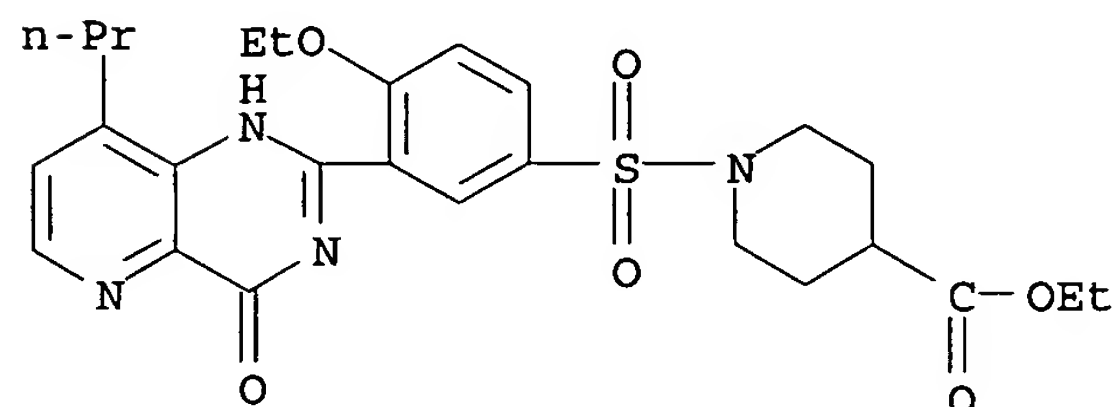
AB The invention relates to the use of a cyclic guanosine 3',5'-monophosphate phosphodiesterase type five (cGMP PDE V) inhibitor for increasing fecundity in a mammal by one or more of (a) promoting the growth of an oocyte, zygote, blastocyst, embryo and/or fetus, (b) increasing the rate or probability of survival of an embryo and/or fetus and (c) increasing the birth weight of a progeny, or for increasing milk productivity. I.v. and tablet formulations are exemplified. Formulations and packs containing the PDE V inhibitors for pharmaceutical or veterinary use are claimed.

IT 155879-56-4 224785-86-8 224786-98-5  
 224787-20-6 224787-26-2 224787-70-6  
 224787-95-5 224788-35-6 224788-38-9  
 224788-62-9 264912-89-2 264913-07-7  
 264913-09-9

RL: AGR (Agricultural use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (use of PDE V inhibitors for improved fecundity in mammals)

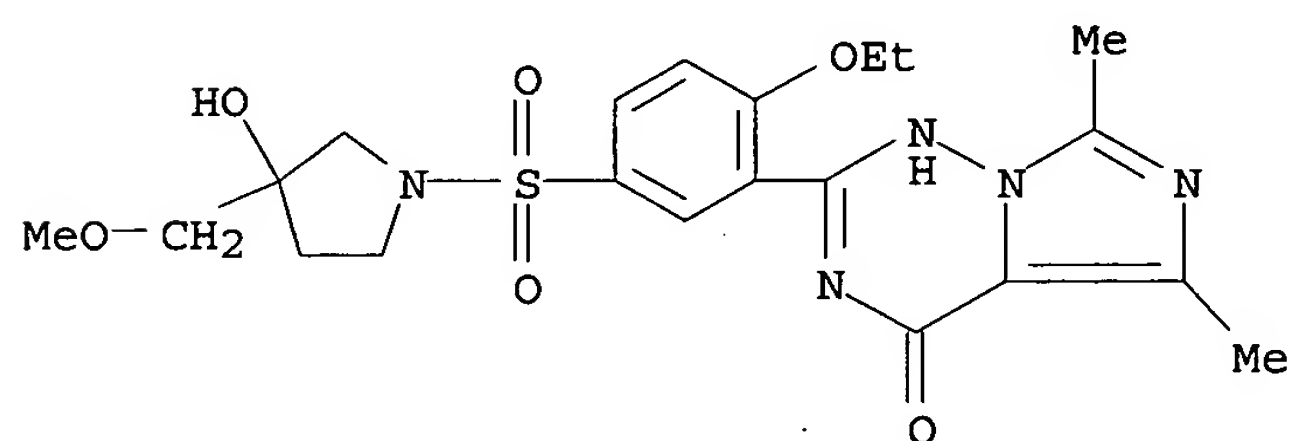
RN 155879-56-4 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[3-(1,4-dihydro-4-oxo-8-propylpyrido[3,2-d]pyrimidin-2-yl)-4-ethoxyphenyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)



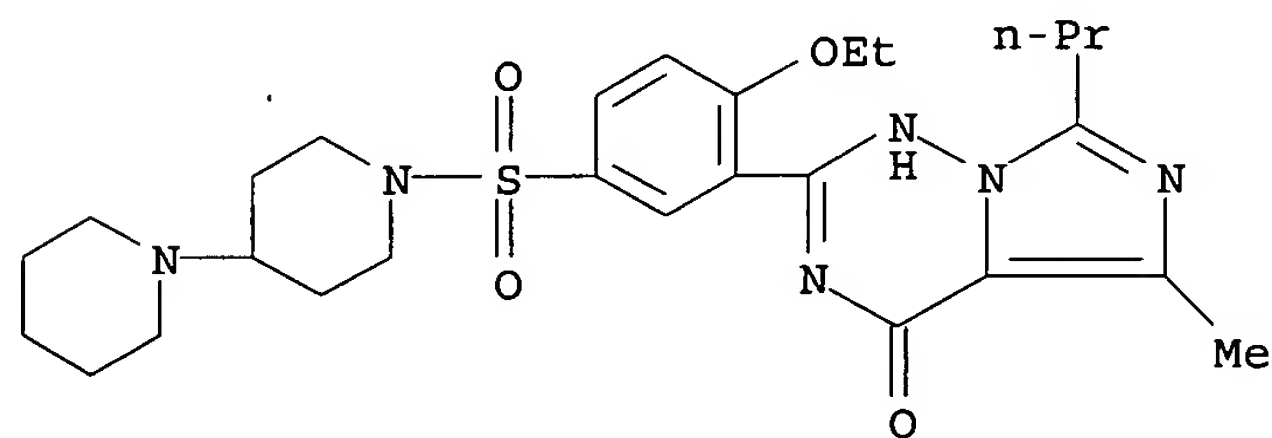
RN 224785-86-8 HCAPLUS

CN 3-Pyrrolidinol, 1-[[3-(1,4-dihydro-5,7-dimethyl-4-oxoimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-3-(methoxymethyl)- (9CI) (CA INDEX NAME)



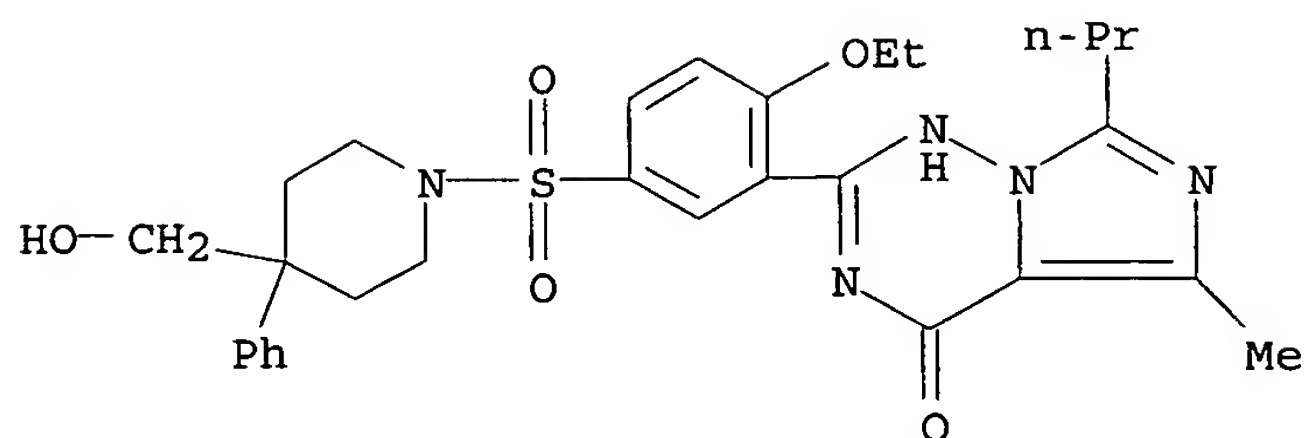
RN 224786-98-5 HCAPLUS

CN 1,4'-Bipiperidine, 1'-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]- (9CI) (CA INDEX NAME)



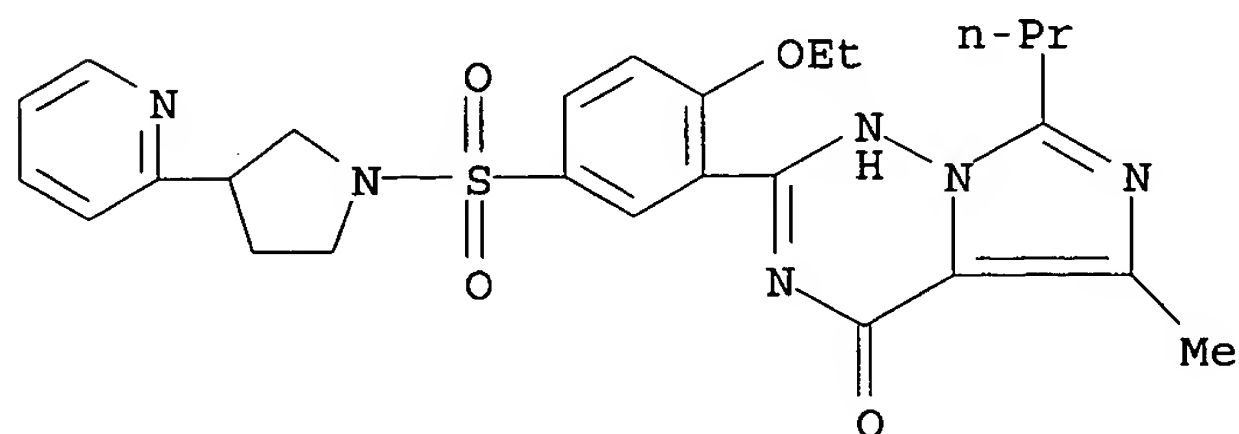
RN 224787-20-6 HCAPLUS

CN 4-Piperidinemethanol, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)



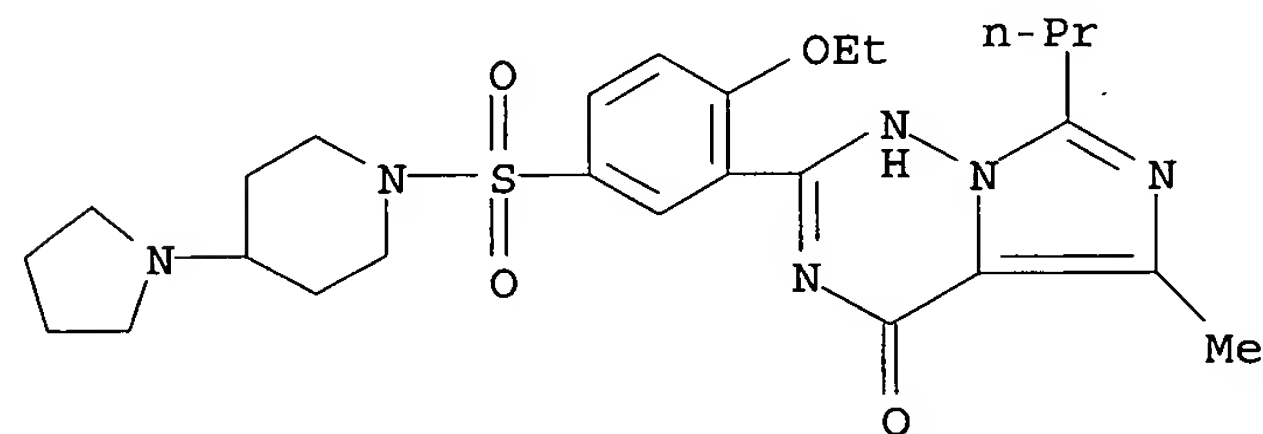
RN 224787-26-2 HCAPLUS

CN Pyrrolidine, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-3-(2-pyridinyl)- (9CI)  
(CA INDEX NAME)



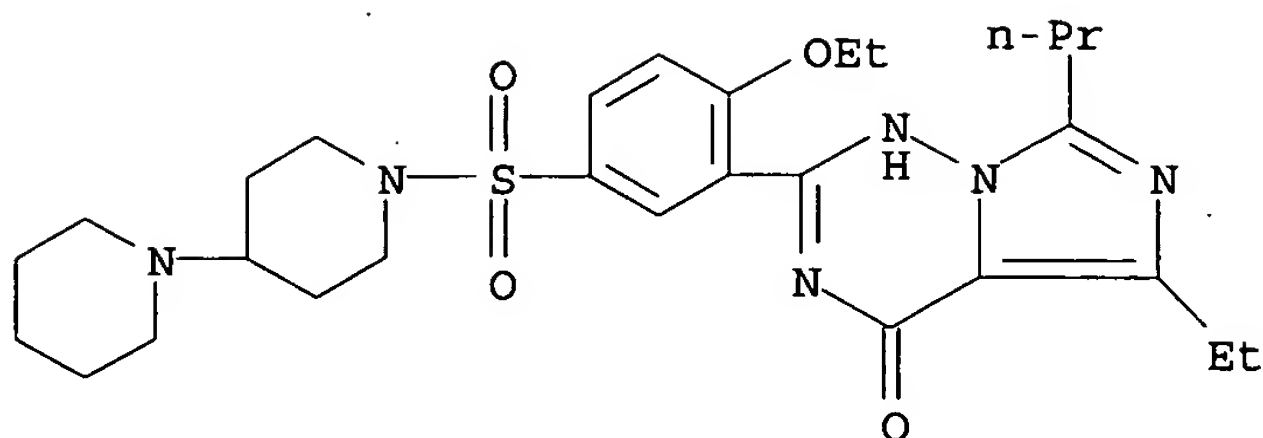
RN 224787-70-6 HCAPLUS

CN Piperidine, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-(1-pyrrolidinyl)- (9CI)  
(CA INDEX NAME)



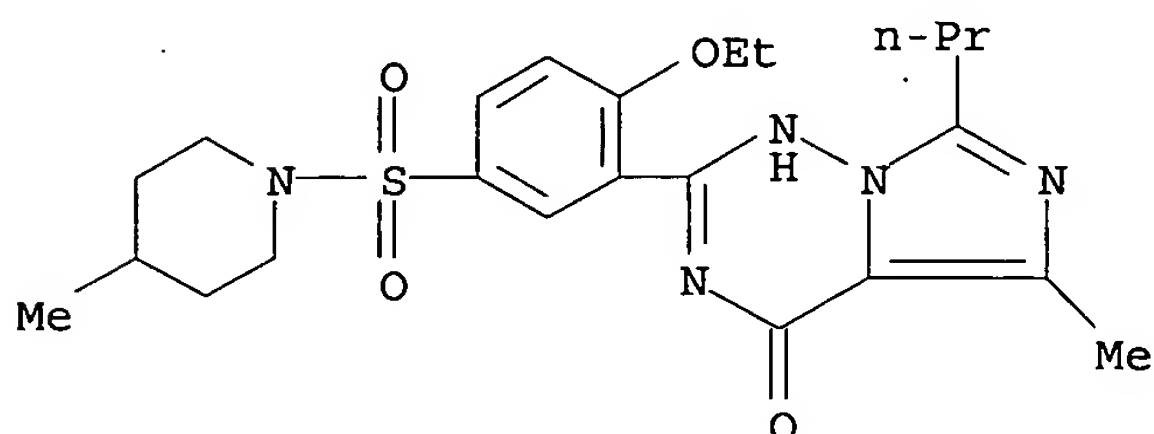
RN 224787-95-5 HCAPLUS

CN 1,4'-Bipiperidine, 1'-[[4-ethoxy-3-(5-ethyl-1,4-dihydro-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



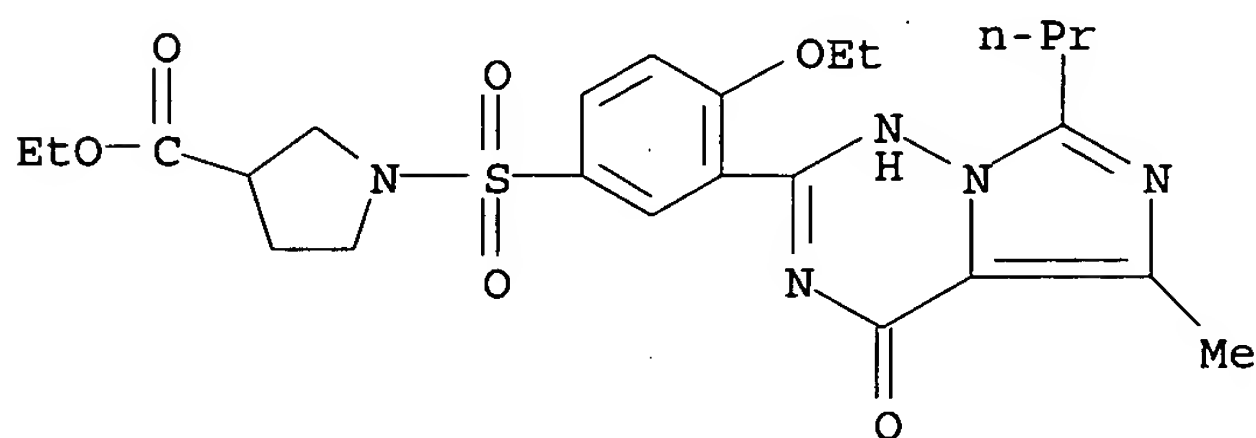
RN 224788-35-6 HCAPLUS

CN Piperidine, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)



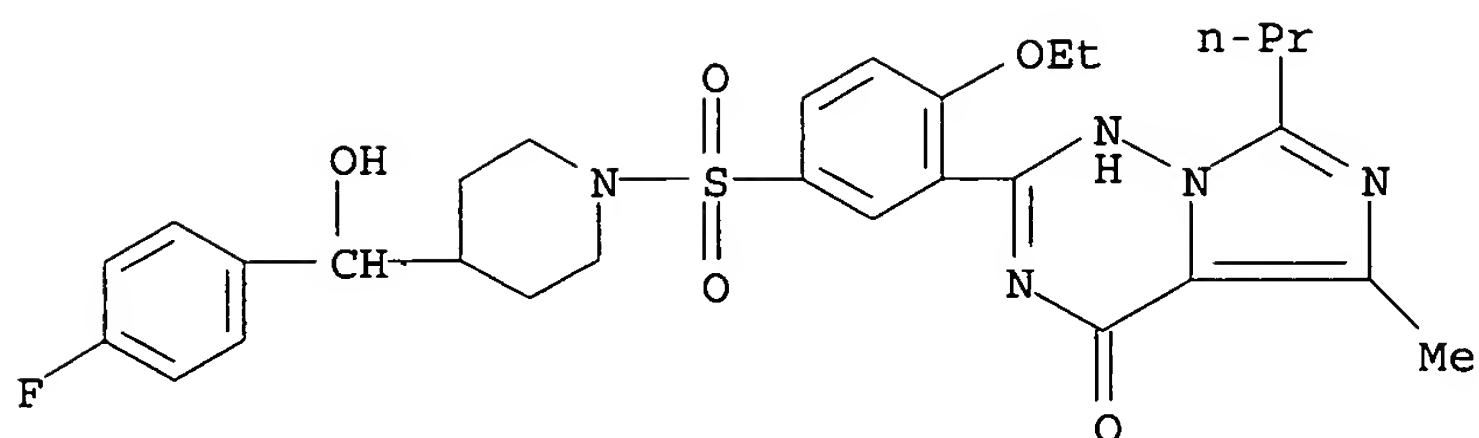
RN 224788-38-9 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)



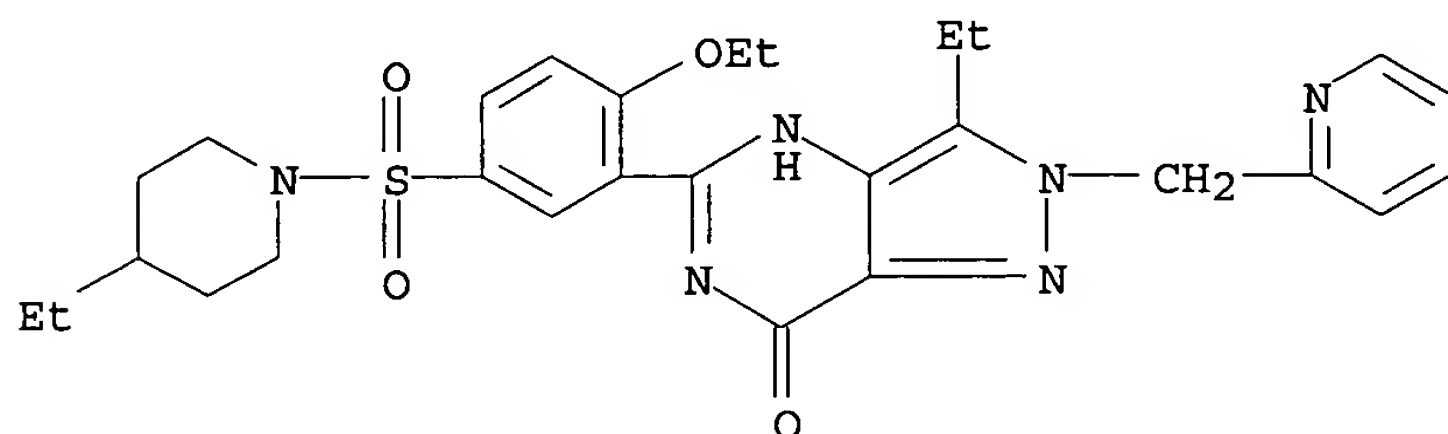
RN 224788-62-9 HCAPLUS

CN 4-Piperidinemethanol, 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-α-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



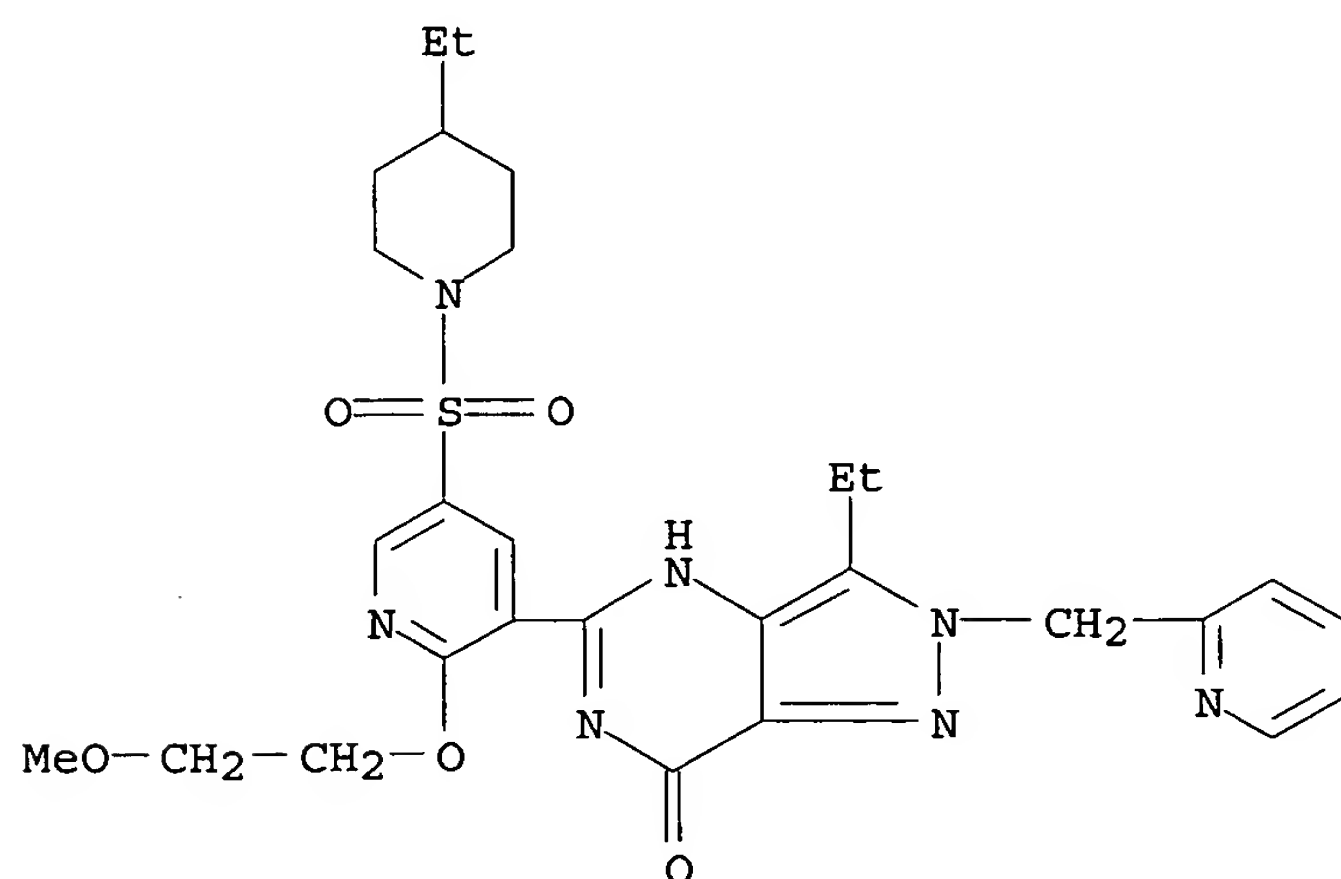
RN 264912-89-2 HCAPLUS

CN Piperidine, 1-[[4-ethoxy-3-[3-ethyl-4,7-dihydro-7-oxo-2-(2-pyridinylmethyl)-2H-pyrazolo[4,3-d]pyrimidin-5-yl]phenyl]sulfonyl]-4-ethyl-(9CI) (CA INDEX NAME)



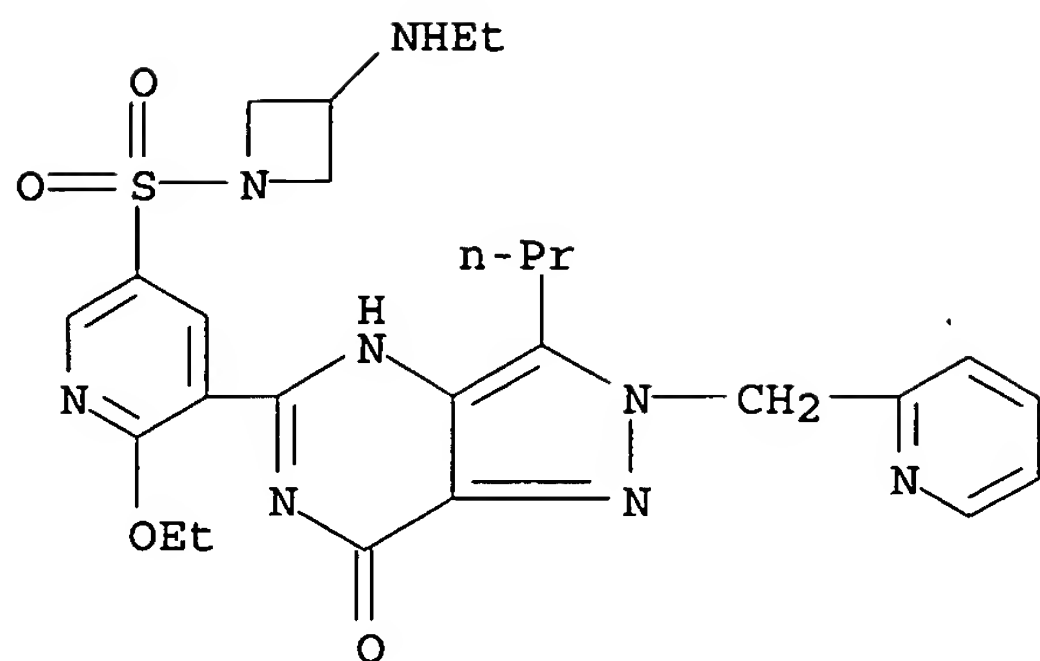
RN 264913-07-7 HCAPLUS

CN Piperidine, 4-ethyl-1-[[5-[3-ethyl-4,7-dihydro-7-oxo-2-(2-pyridinylmethyl)-2H-pyrazolo[4,3-d]pyrimidin-5-yl]-6-(2-methoxyethoxy)-3-pyridinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 264913-09-9 HCAPLUS

CN 3-Azetidinamine, 1-[[5-[4,7-dihydro-7-oxo-3-propyl-2-(2-pyridinylmethyl)-2H-pyrazolo[4,3-d]pyrimidin-5-yl]-6-ethoxy-3-pyridinyl]sulfonyl]-N-ethyl-(9CI) (CA INDEX NAME)



L32 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:213823 HCAPLUS

DOCUMENT NUMBER: 136:247500

TITLE: Preparation of alkynyloxyphenylsulfonylmethylpiperidin  
ehydroxamic acids and related compounds as  
inhibitors of matrix metalloproteinase and  
TNF- $\alpha$  converting enzyme (TACE).

INVENTOR(S): Levin, Jeremy I.; Venkatesan, Aranapakam M.; Chen,  
James M.; Zask, Arie; Sandanayaka, Vincent P.; Du,  
Mila T.; Baker, Jannie L.

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: U.S., 50 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6358980	B1	20020319	US 2000-492686	20000127 <--
US 2002086890	A1	20020704	US 2001-29655	20011221 <--
US 6753337	B2	20040622		
US 2004229924	A1	20041118	US 2004-870839	20040617
PRIORITY APPLN. INFO.:			US 1999-155184P	P 19990127
			US 2000-492686	A3 20000127
			US 2001-29655	A1 20011221

OTHER SOURCE(S): MARPAT 136:247500

AB R1C.tplbond.CCR2R3XYACR8R9(CR10R11)nCONR12OH (R1 = H, aryl, heteroaryl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl; R2, R3 = H, alkyl, cyano, CCH; R8-R11 = H, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, alkyl, alkenyl, alkynyl; 1 of R8R9, R9R10, or R10R11 = atoms to form a cycloalkyl ring or a cycloheteroalkyl ring; R12 = H, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, alkyl; A, X = O, S, SO, SO<sub>2</sub>, NR<sub>7</sub>, CH<sub>2</sub>; R<sub>7</sub> = H, aryl, aralkyl, heteroaryl, heteroaralkyl, etc.; Y = aryl, heteroaryl; A and X are not bonded to adjacent atoms of Y; n = 0-2), were prepared Thus, 1-acetyl-4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-4-piperidinecarboxamide (preparation in several steps from Et isonipecotate given) inhibited TACE with IC<sub>50</sub> = 4.8 nM.

IT 287201-30-3P, 4-Piperidinecarboxamide, 4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-1-[(1-methyl-1H-pyrazol-4-yl)sulfonyl]-

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

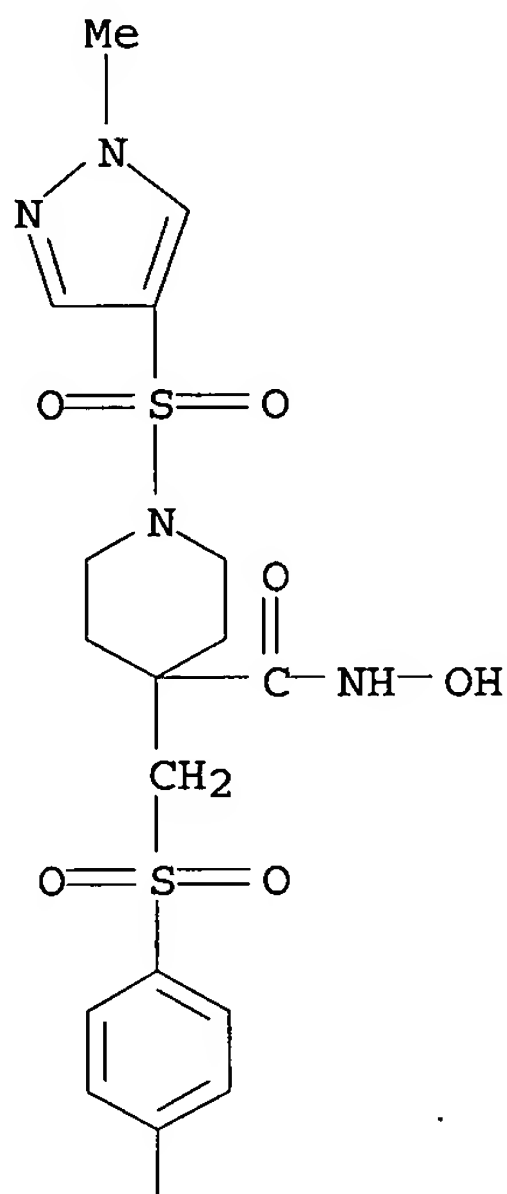
## (Uses)

(preparation of alkynyloxyphenylsulfonylmethylpiperidinehydroxamic acids and related compds. as **inhibitors** of matrix metalloproteinase and TNF- $\alpha$  converting **enzyme** (TACE))

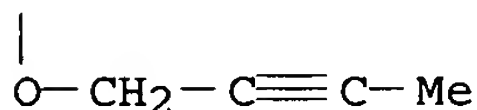
RN 287201-30-3 HCAPLUS

CN 4-Piperidinecarboxamide, 4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-1-[(1-methyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



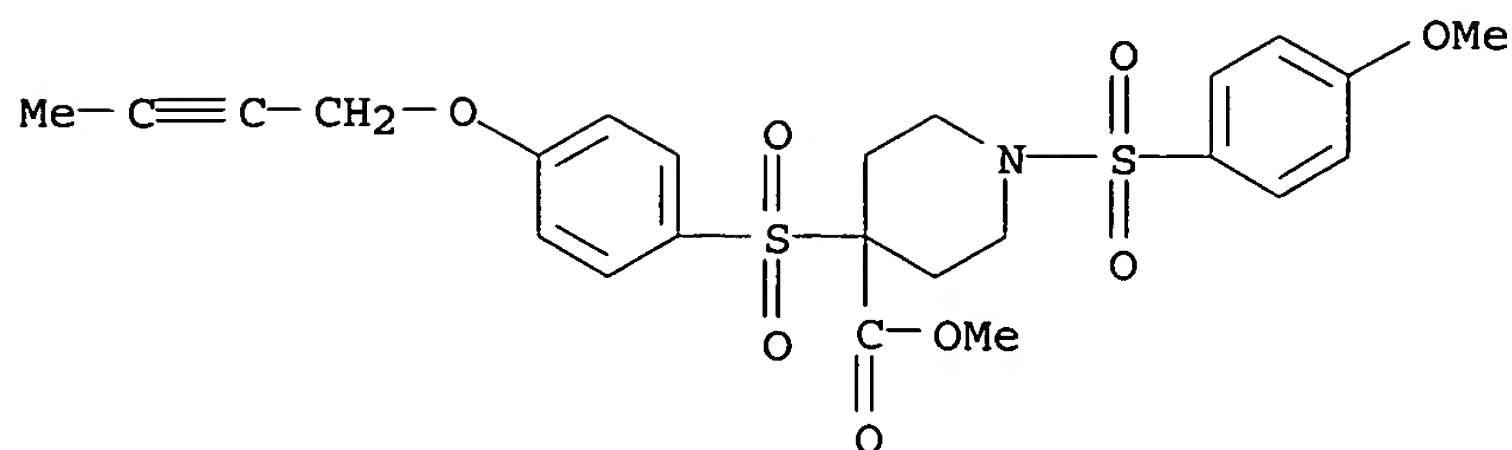
IT **287202-66-8P**, 4-Piperidinecarboxylic acid, 4-[[[4-(2-butynyloxy)phenyl]sulfonyl]-1-[(4-methoxyphenyl)sulfonyl]-, methylester  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of alkynyloxyphenylsulfonylmethylpiperidinehydroxamic acids and related compds. as **inhibitors** of matrix metalloproteinase and TNF- $\alpha$  converting **enzyme** (TACE))

RN 287202-66-8 HCAPLUS

CN 4-Piperidinecarboxylic acid, 4-[[[4-(2-butynyloxy)phenyl]sulfonyl]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:171694 HCAPLUS

DOCUMENT NUMBER: 136:232208

TITLE: Preparation of 4-aminoazepan-3-one parasitic cysteine protease inhibitors effective against malaria and other diseases

INVENTOR(S): Tew, David G.; Thompson, Scott K.; Veber, Daniel F.

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, UK

SOURCE: PCT Int. Appl., 220 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

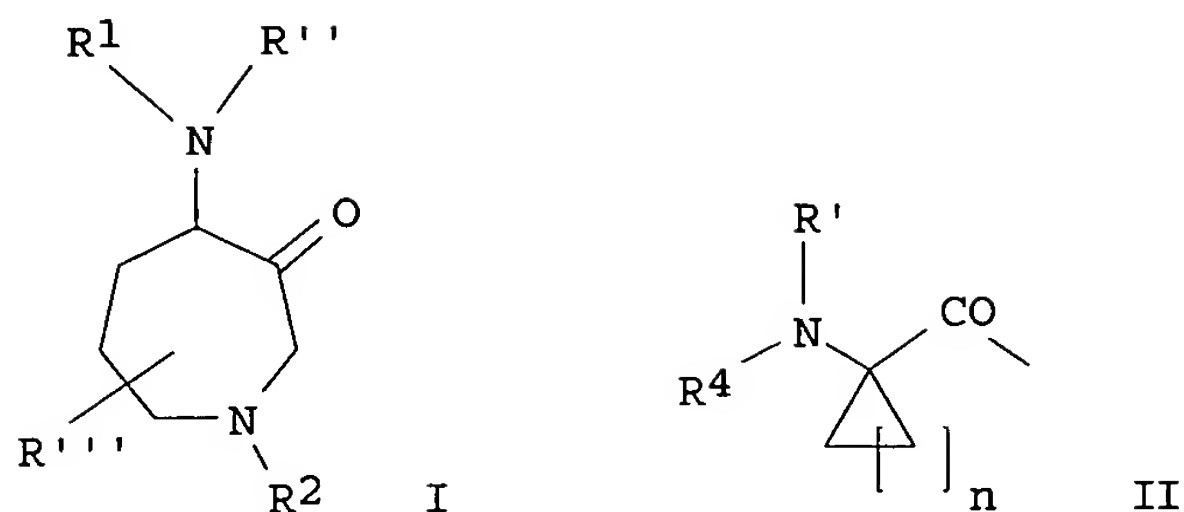
FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017924	A1	20020307	WO 2001-US27178	20010831 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003144175	A1	20030731	US 2001-881334	20010614 <--
AU 2001086983	A5	20020313	AU 2001-86983	20010831 <--
EP 1320370	A1	20030625	EP 2001-966474	20010831 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509083	T2	20040325	JP 2002-522897	20010831
PRIORITY APPLN. INFO.:				
			US 2000-653815	A2 20000901
			US 2001-881334	A2 20010614
			US 1998-113636P	P 19981223
			US 1999-164581P	P 19991110
			WO 1999-US30730	A2 19991221
			US 2000-593845	B2 20000614
			WO 2001-US27178	W 20010831

OTHER SOURCE(S): MARPAT 136:232208

GI



AB The present invention relates to methods of treating parasitic diseases which are mediated by cysteine proteases by administration of 4-aminoazepan-3-one protease inhibitors I (e.g. benzo[1,3]dioxole-5-carboxylic acid [(S)-1-(1-benzyl-3-oxoazepan-4-ylcarbamoyl)-3-methylbutyl]amide) and pharmaceutically acceptable salts, hydrates and solvates thereof. In particular, the present invention relates to a method of treating malaria by inhibiting the cysteine protease falcipain. Other diseases against which the claimed compds. are effective include trypanosomiasis (African sleeping sickness, Chagas disease), leishmaniasis, schistosomiasis, onchocerciasis (river blindness) and giardiasis. In I: R1 is R4NR'CHR3C(O)-, R5XCHR3C(O)-, R3CH2C(O)-, R4NR'CR''R3C(O)-, II. R2 is H, C1-6alkyl, C3-6cycloalkyl-CO-6alkyl, Ar-CO-6alkyl, Het-CO-6alkyl, R9C(O)-, R9C(S)-, R9SO2-, R9OC(O)-, R9R11NC(O)-, R9R11NC(S)-, R9(R11)NSO2-, 3-(2-pyridyl)benzylcarbonyl, 2-(3-(2-pyridyl)phenyl)ethyl, R7NR6CHR8Z-, and R9SO2R11NC(O)-. R3 is H, C1-6alkyl, C3-6cycloalkyl-CO-6alkyl, C2-6alkenyl, C2-6alkynyl, HetCO-6alkyl and ArCO-6alkyl. R3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring. R4 is H, C1-6alkyl, C3-6cycloalkyl-CO-6alkyl, Ar-CO-6alkyl, Het-CO-6alkyl, R5C(O)-, R5C(S)-, R5SO2-, R5OC(O)-, R5R12NC(O)-, and R5R12NC(S)-. R5 is H, C1-6alkyl, C2-6alkenyl, C2-6alkynyl, C3-6cycloalkyl-CO-6alkyl, Ar-CO-6alkyl and Het-CO-6alkyl. R6 is H, C1-6alkyl, Ar-CO-6alkyl, and Het-CO-6alkyl. R7 is H, C1-6alkyl, C3-6cycloalkyl-CO-6alkyl, Ar-CO-6alkyl, Het-CO-6alkyl, R10C(O)-, R10C(S)-, R10SO2-, R10OC(O)-, R10R13NC(O)-, and R10R13NC(S)-. R8 is H, C1-6alkyl, C2-6alkenyl, C2-6alkynyl, HetCO-6alkyl and ArCO-6alkyl. R9, R10 independently = C1-6alkyl, C3-6cycloalkyl-CO-6alkyl, Ar-CO-6alkyl and Het-CO-6alkyl. R11, R12, R13, R', R'' independently = H, C1-6alkyl, Ar-CO-6alkyl, and Het-CO-6alkyl. R''' is H, C1-6alkyl, C3-6cycloalkyl-CO-6alkyl, Ar-CO-6alkyl, and Het-CO-6alkyl; R'''' is C1-6alkyl, C3-6cycloalkyl-CO-6alkyl C2-6alkenyl, C2-6alkynyl, HetCO-6alkyl and ArCO-6alkyl. X is CH2, S, and O; Z is C(O) and CH2; n is 1-5. Although the methods of preparation are not claimed, 220 example preps. are included.

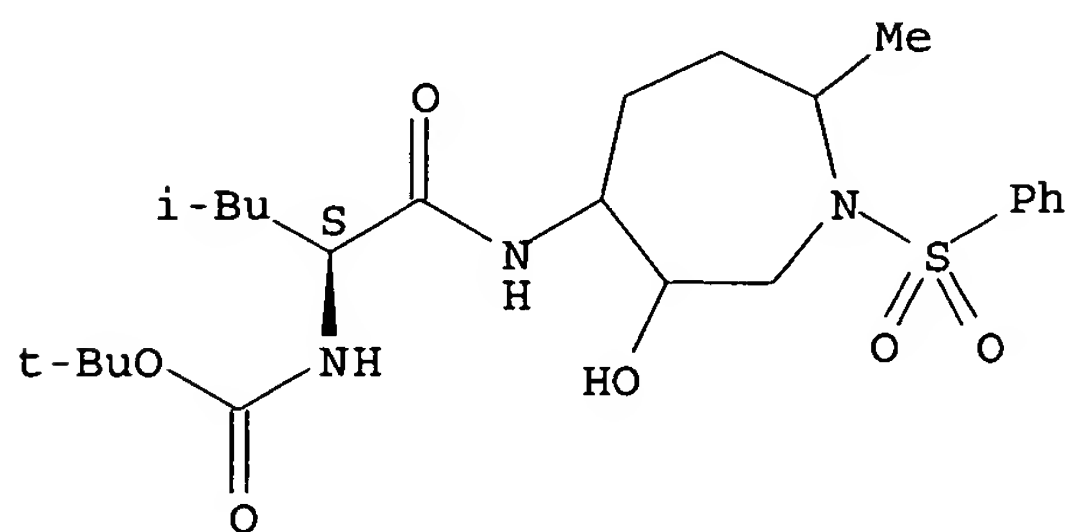
IT **403700-46-9P**, [(1S)-1-[(1-Benzenesulfonyl-3-hydroxy-7-methylazepan-4-yl)carbamoyl]-3-methylbutyl]carbamic acid tert-butyl ester  
**403700-47-0P**, (S)-2-Amino-4-methylpentanoic acid  
 [1-(2-pyridine)sulfonyl-3-hydroxy-7-methylazepan-4-yl]amide  
**403700-48-1P**, Benzofuran-2-carboxylic acid [(1S)-1-[[3-hydroxy-7-methyl-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]-3-methylbutyl]amide  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (intermediate; preparation of 4-aminoazepan-3-one parasitic cysteine protease **inhibitors** effective against malaria and other diseases)

RN 403700-46-9 HCAPLUS

CN Carbamic acid, [(1S)-1-[[[hexahydro-3-hydroxy-7-methyl-1-(phenylsulfonyl)-

1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-, 1,1-dimethylethyl ester  
(9CI) (CA INDEX NAME)

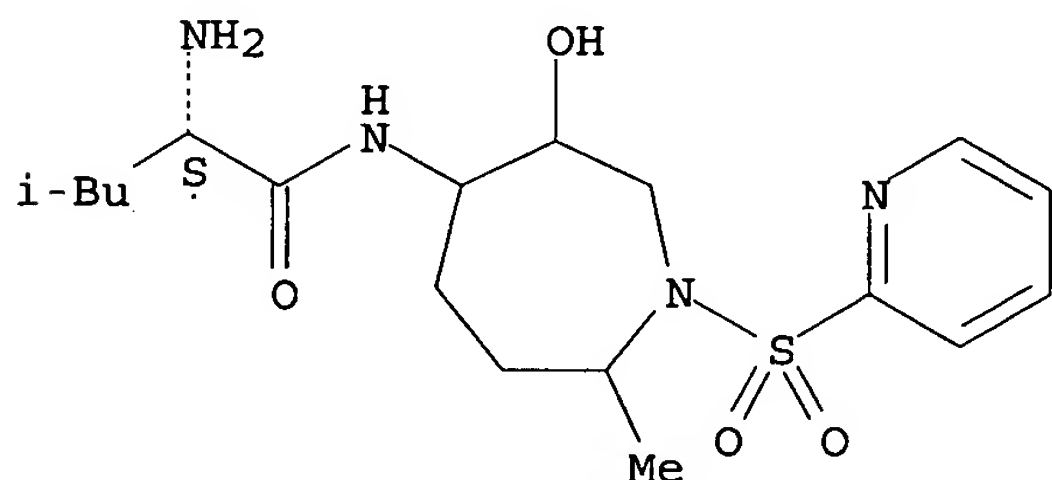
Absolute stereochemistry.



RN 403700-47-0 HCAPLUS

CN Pentanamide, 2-amino-N-[hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

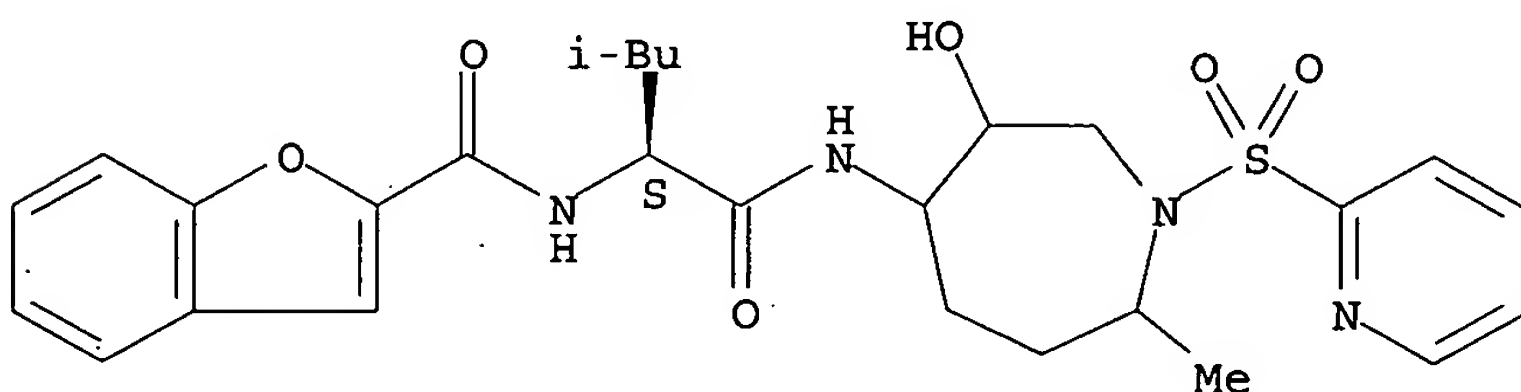
Absolute stereochemistry.



RN 403700-48-1 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-3-hydroxy-7-methyl-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



IT 281215-23-4P, 5,6-Dimethoxybenzofuran-2-carboxylic acid  
[(1S)-3-methyl-1-[[[3-oxo-1-(1-methyl-1H-imidazole-4-sulfonyl)azepan-4-yl]carbamoyl]butyl]amide 281215-25-6P, Benzofuran-2-carboxylic acid  
[(1S)-3-methyl-1-[[[1-(1-methyl-1H-imidazole-2-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide 281215-28-9P, Benzofuran-2-carboxylic acid  
[(1S)-3-methyl-1-[[[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide 281215-33-6P, 5-Hydroxybenzofuran-2-carboxylic acid  
[(1S)-3-methyl-1-[[[1-(1-methyl-1H-imidazole-4-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide 281216-87-3P,

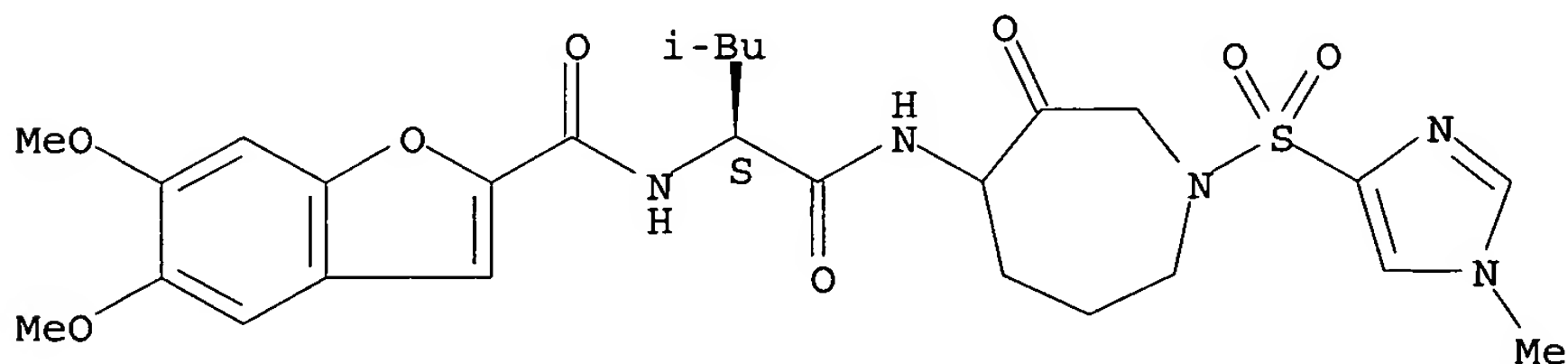
Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[1-(6-methylpyridin-2-ylsulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide **281216-98-6P**, Thieno[3,2-b]thiophene-2-carboxylic acid [(1S)-3-methyl-1-[[1-(3-methylpyridine-2-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide **281216-99-7P**, 3-Methylbenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[1-(3-methylpyridin-2-ylsulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide **281217-04-7P**, Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridinesulfonyl)azepan-4-yl]carbamoyl]butyl]amide **362505-86-0P**, Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[4S,7S)-7-methyl-3-oxo-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide **362505-88-2P**, Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[4R,7R)-7-methyl-3-oxo-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide **403606-21-3P**, 5-Methoxybenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[4R)-1-(3-methylpyridin-2-ylsulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide **403606-31-5P**, Benzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[1-(2-methylfuran-3-sulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide **403606-46-2P**, Benzo[b]thiophene-2-carboxylic acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide **403606-47-3P**, 5-Methoxybenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide **403606-48-4P**, 3-Methylbenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide **403606-49-5P**, Thieno[3,2-b]thiophene-2-carboxylic acid [(1S)-3-methyl-1-[[6-methyl-3-oxo-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]butyl]amide **403606-64-4P**, 5-Methoxybenzofuran-2-carboxylic acid [(1S)-3-methyl-1-[[4S)-1-(3-methylpyridin-2-ylsulfonyl)-3-oxoazepan-4-yl]carbamoyl]butyl]amide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-aminoazepan-3-one parasitic cysteine protease inhibitors effective against malaria and other diseases)

RN 281215-23-4 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5,6-dimethoxy- (9CI) (CA INDEX NAME)

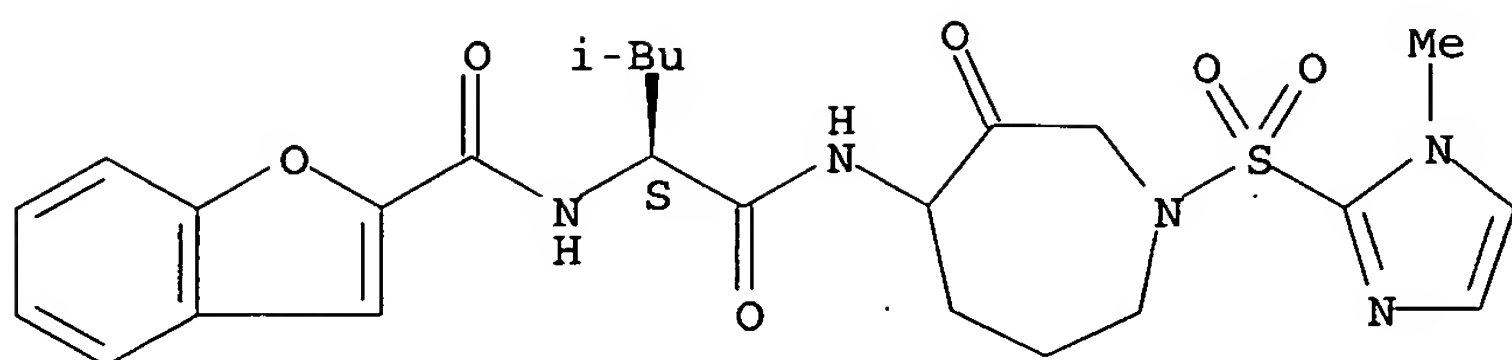
Absolute stereochemistry.



RN 281215-25-6 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-methyl-1H-imidazol-2-yl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

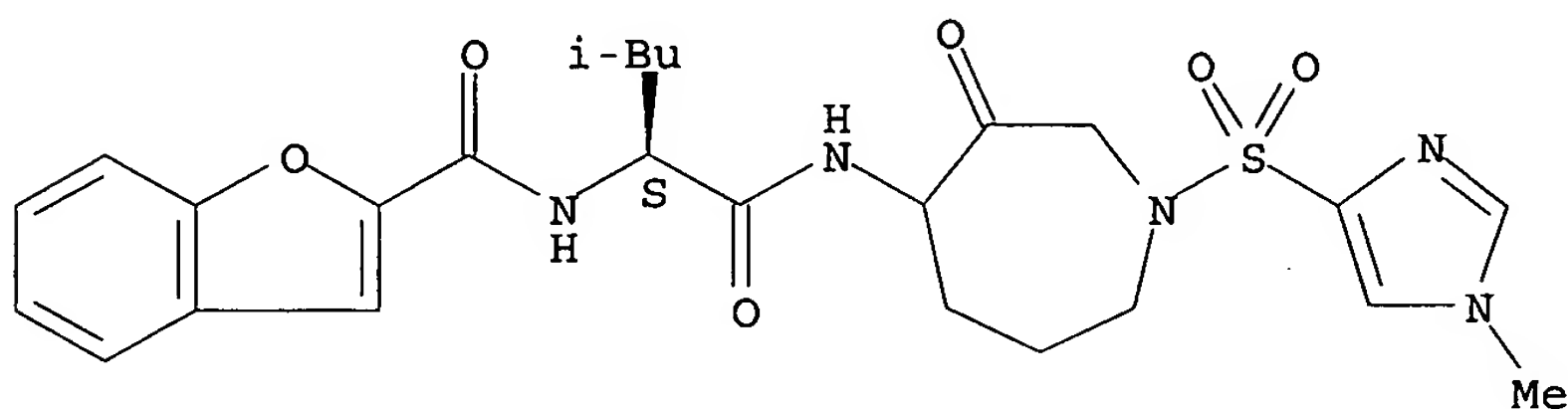
Absolute stereochemistry.



RN 281215-28-9 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI)  
(CA INDEX NAME)

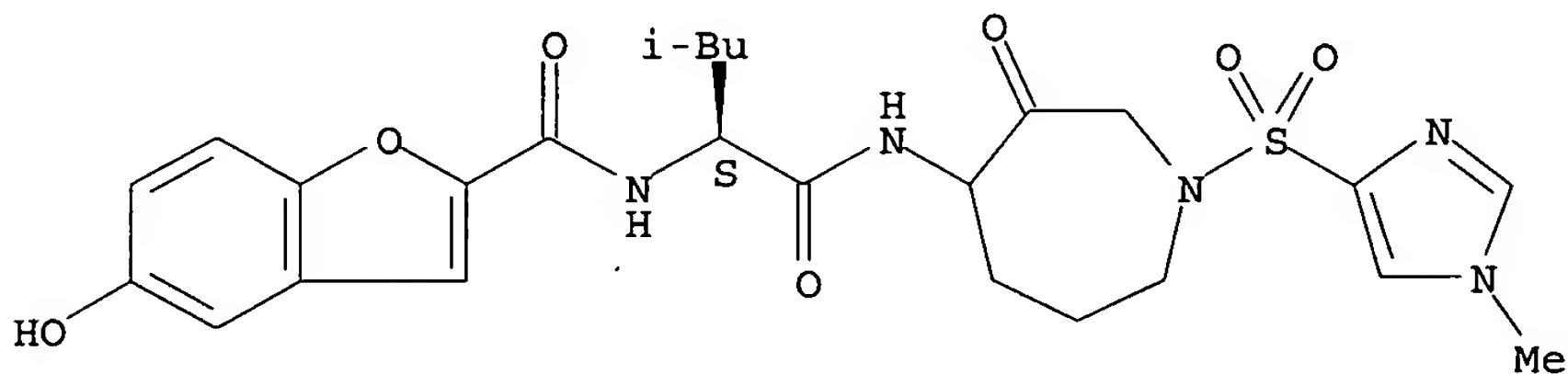
Absolute stereochemistry.



RN 281215-33-6 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-hydroxy- (9CI) (CA INDEX NAME)

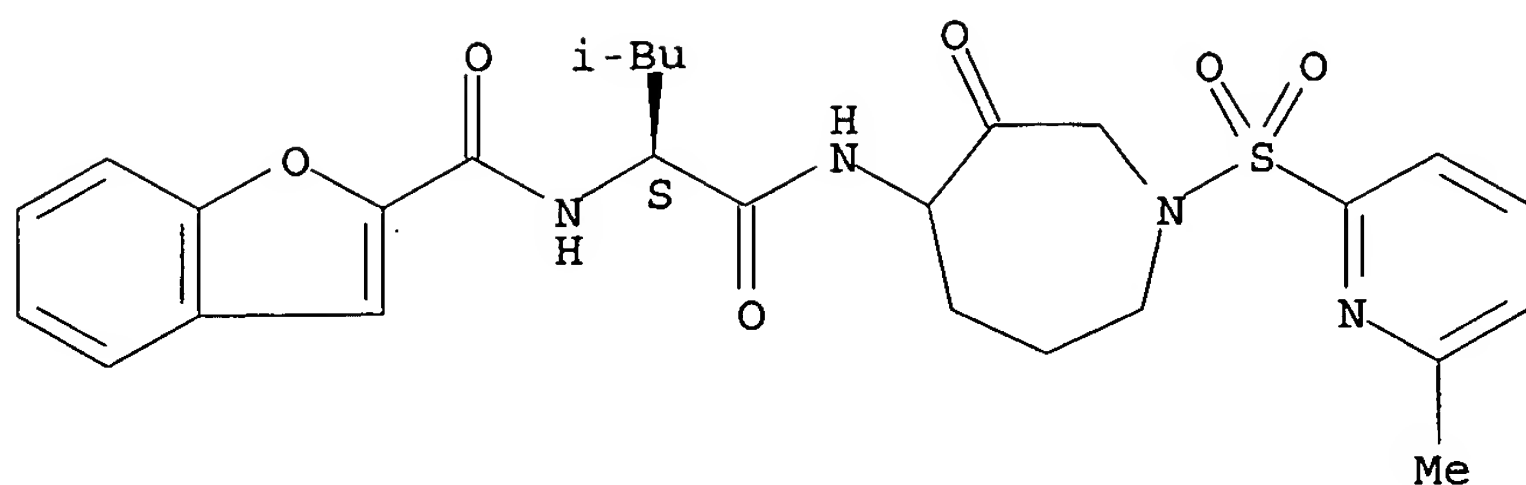
Absolute stereochemistry.



RN 281216-87-3 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(6-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

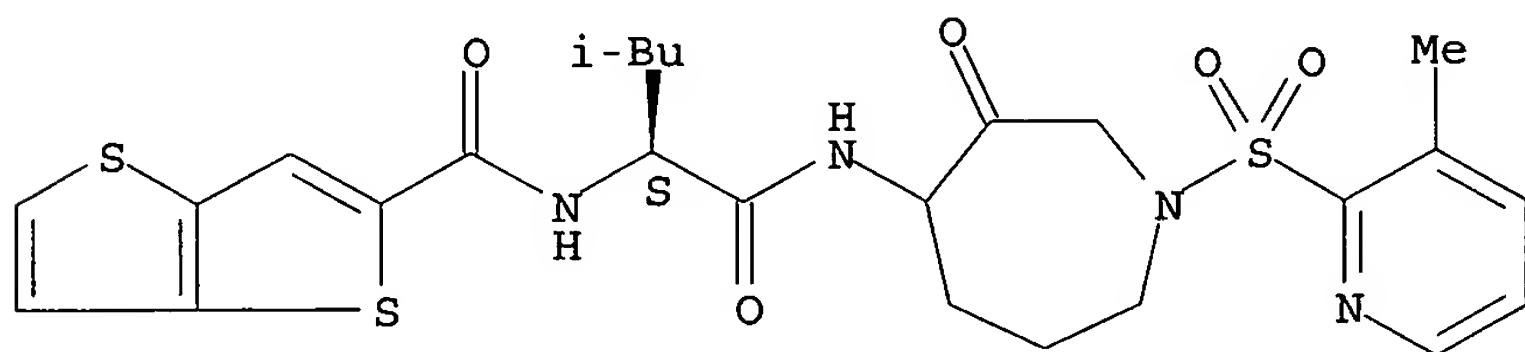
Absolute stereochemistry.



RN 281216-98-6 HCAPLUS

CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-1-[(3-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

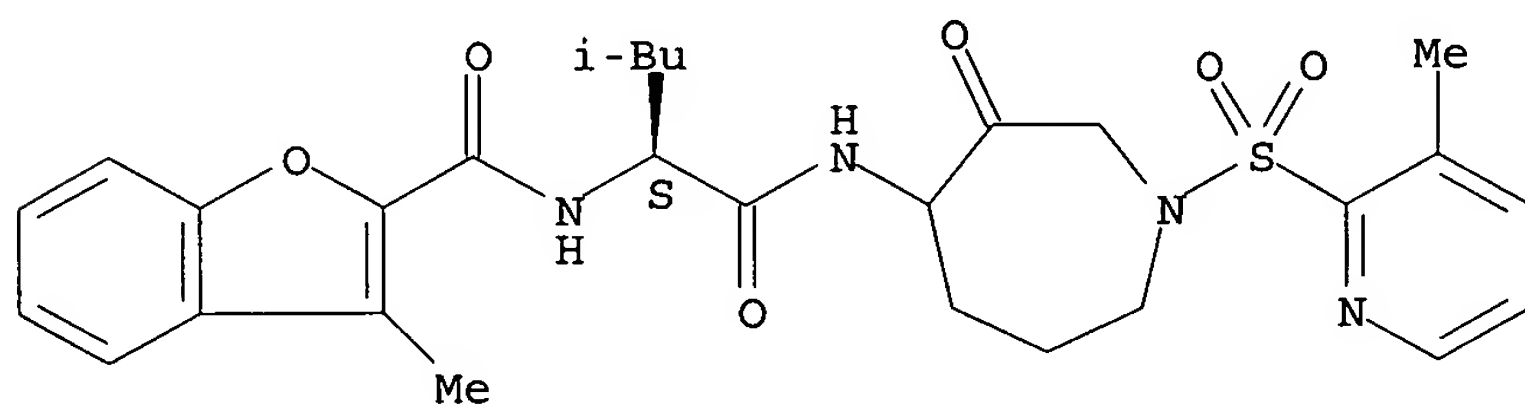
Absolute stereochemistry.



RN 281216-99-7 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(3-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

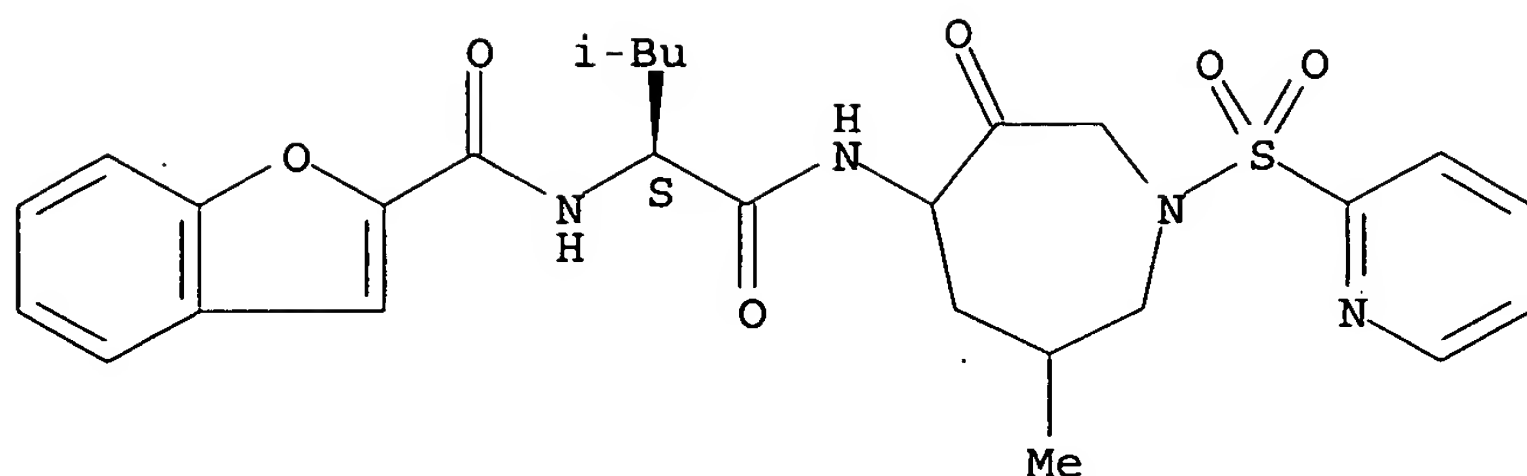
Absolute stereochemistry.



RN 281217-04-7 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

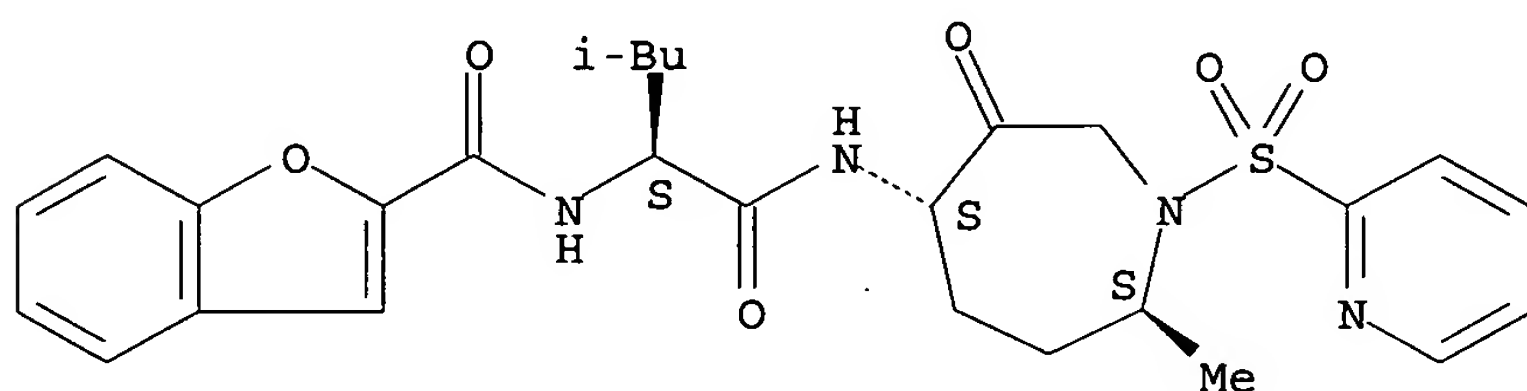
Absolute stereochemistry.



RN 362505-86-0 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S,7S)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI)  
(CA INDEX NAME)

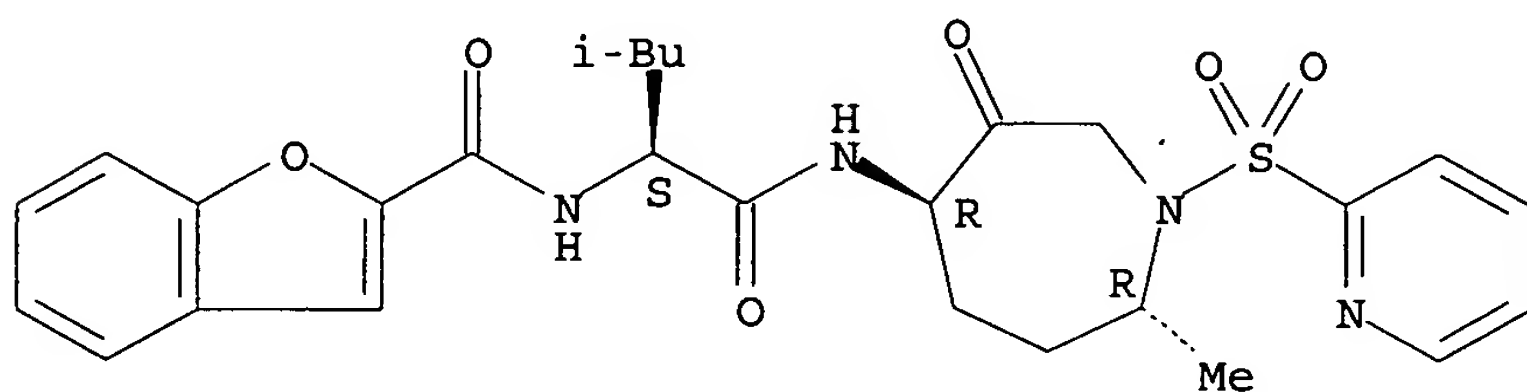
Absolute stereochemistry.



RN 362505-88-2 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R,7R)-hexahydro-7-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI)  
(CA INDEX NAME)

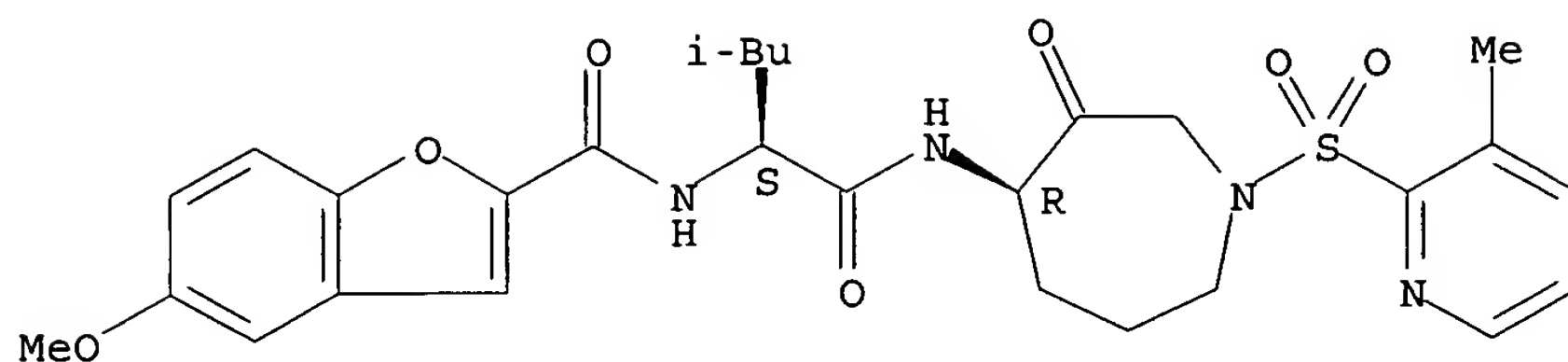
Absolute stereochemistry.



RN 403606-21-3 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4R)-hexahydro-1-[(3-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

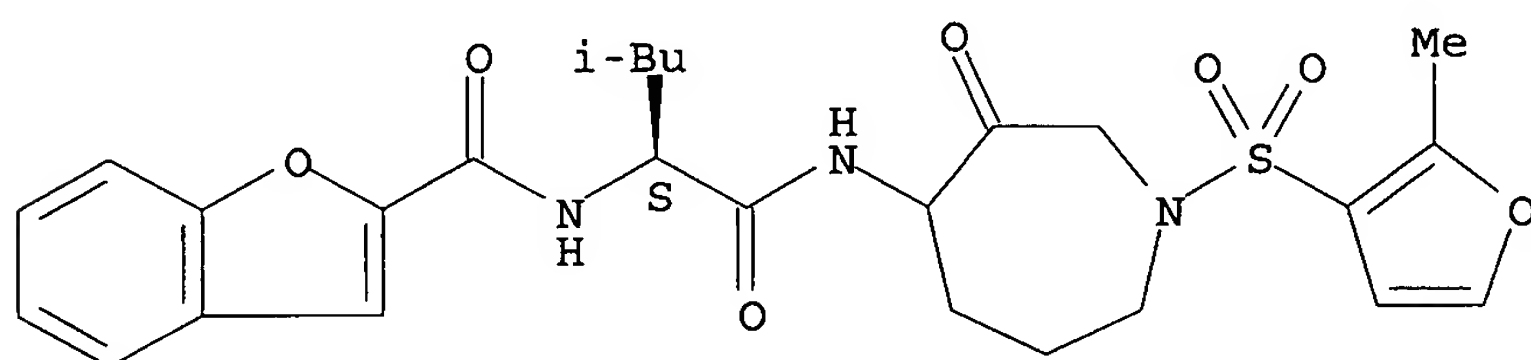
Absolute stereochemistry.



RN 403606-31-5 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-1-[(2-methyl-3-furanyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

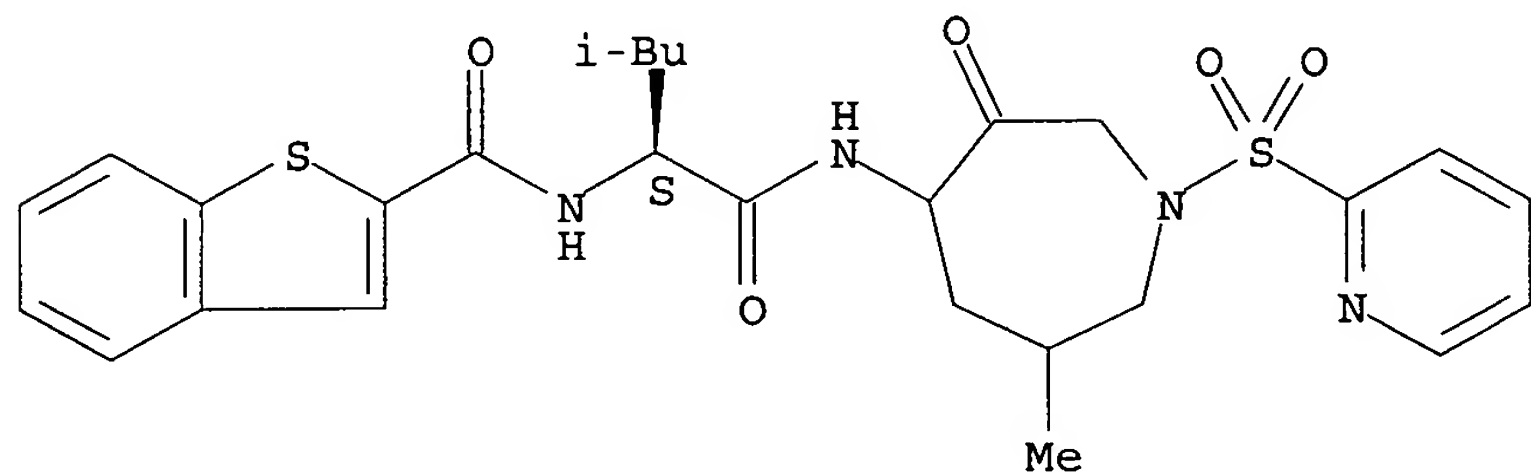
Absolute stereochemistry.



RN 403606-46-2 HCAPLUS

CN Benzo[b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

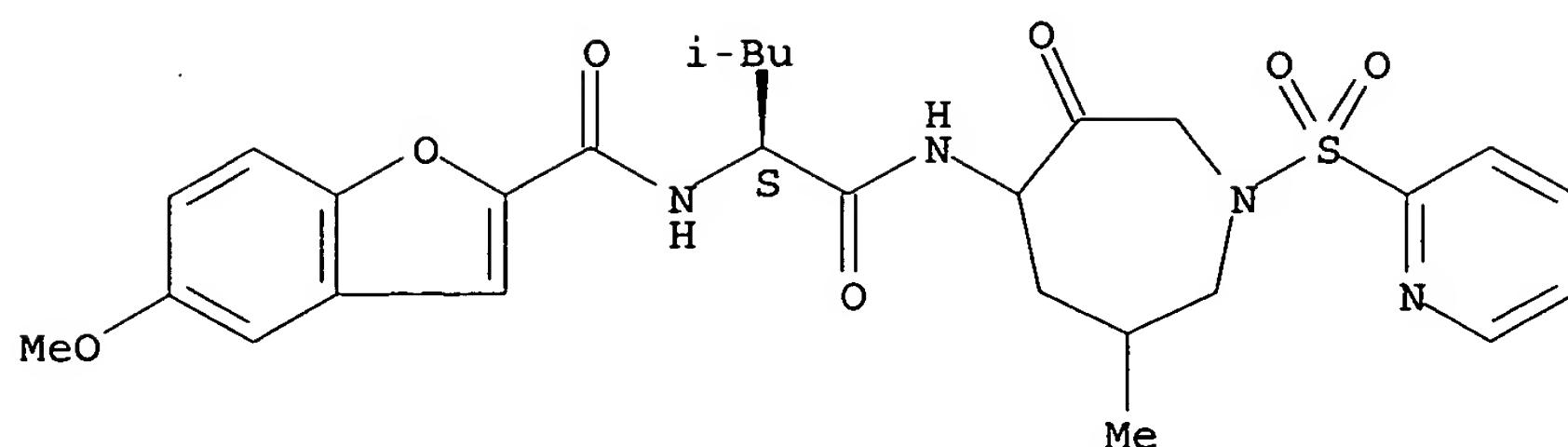


RN 403606-47-3 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

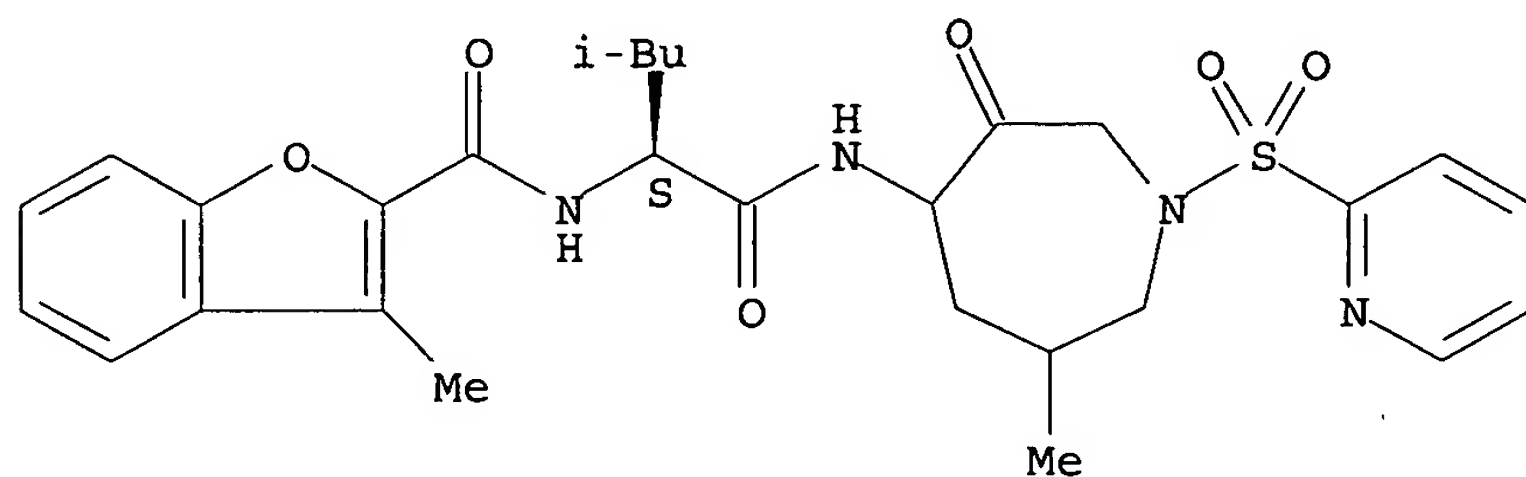




RN 403606-48-4 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

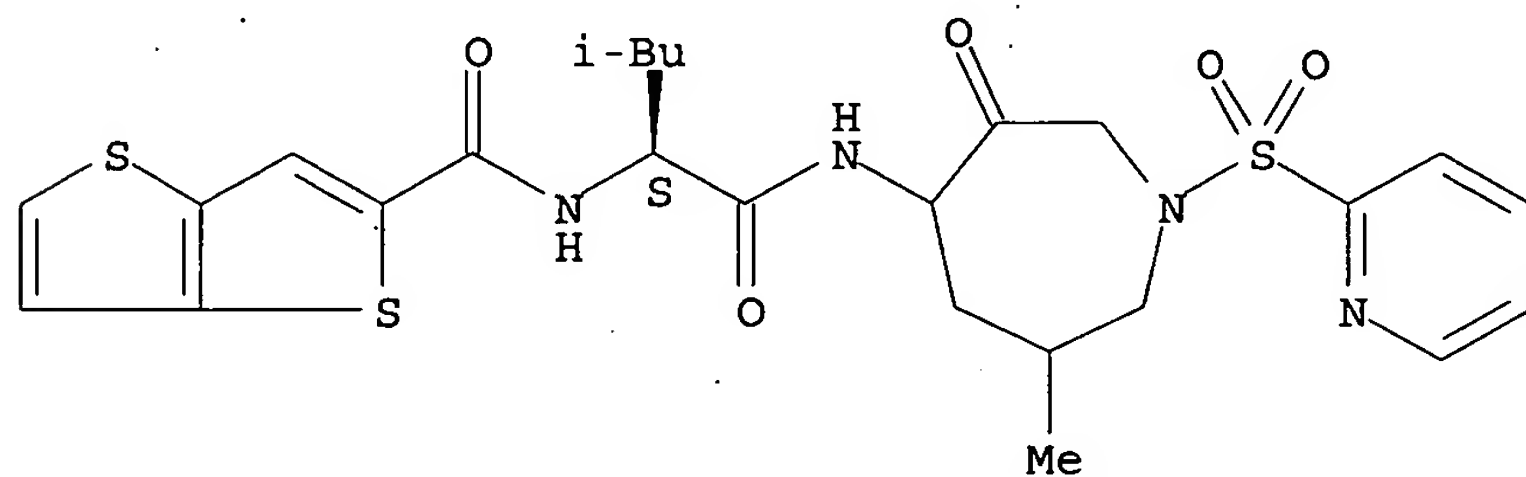
Absolute stereochemistry.



RN 403606-49-5 HCAPLUS

CN Thieno[3,2-b]thiophene-2-carboxamide, N-[(1S)-1-[[[hexahydro-6-methyl-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-3-methyl- (9CI) (CA INDEX NAME)

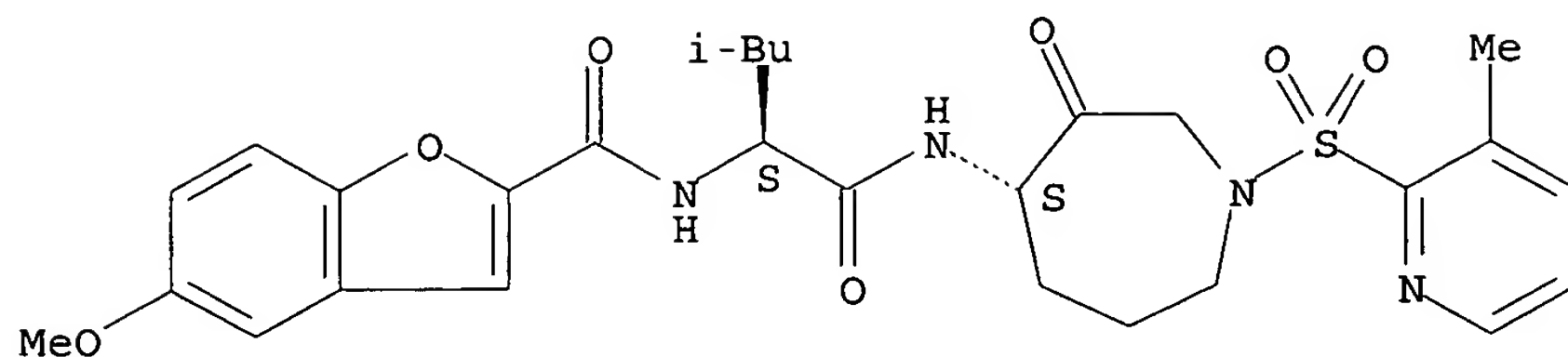
Absolute stereochemistry.



RN 403606-64-4 HCAPLUS

CN 2-Benzofurancarboxamide, N-[(1S)-1-[[[(4S)-hexahydro-1-[(3-methyl-2-pyridinyl)sulfonyl]-3-oxo-1H-azepin-4-yl]amino]carbonyl]-3-methylbutyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:90005 HCAPLUS

DOCUMENT NUMBER: 136:151068

TITLE: Preparation of pyrrolidinethiols and analogs as metalloprotease inhibitors

INVENTOR(S): Aebi, Johannes; Bur, Daniel; Chucholowski, Alexander; Dehmlow, Henrietta; Kitas, Eric Argirios; Obst, Ulrike; Wessel, Hans Peter

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 160 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

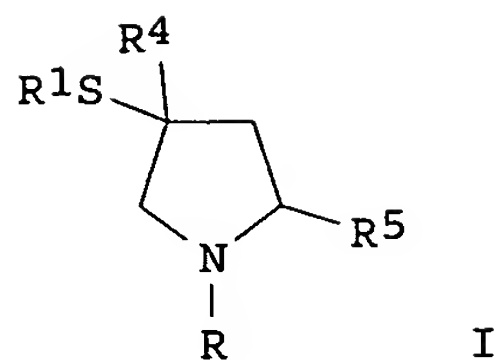
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008185	A1	20020131	WO 2001-EP7951	20010710 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2415740	AA	20020131	CA 2001-2415740	20010710 <--
EP 1303486	A1	20030423	EP 2001-956523	20010710 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012655	A	20030624	BR 2001-12655	20010710 <--
JP 2004504379	T2	20040212	JP 2002-514092	20010710
US 2002040146	A1	20020404	US 2001-906980	20010717 <--
ZA 2003000170	A	20040407	ZA 2003-170	20030107
US 2003199569	A1	20031023	US 2003-373622	20030225 <--
US 6790860	B2	20040914		
US 2004242672	A1	20041202	US 2004-881427	20040630
PRIORITY APPLN. INFO.:			EP 2000-114949	A 20000719
			WO 2001-EP7951	W 20010710
			US 2001-906980	B3 20010717
			US 2003-373622	A3 20030225

OTHER SOURCE(S): MARPAT 136:151068

GI



AB Title compds. [e.g., I; R = Z1R3 or SO3H; R1 = H, alkanoyl, aroyl; R3 = alkyl, (hetero)aryl, heterocyclyl, etc.; R4 = H or alkyl; R5 = CH2Z2R2; R2 = aryl(alkyl), ar(o)ylamino, arylsulfonyl, etc.; Z1 = sulfonyl(amino), CONH, CO2, etc.; Z2 = CH2, O, S, (un)substituted NH] were prepared. Thus, e.g., (3R,5S)-1-naphthalene-2-sulfonyl-5-anilinomethylpyrrolidine-3-thiol was prepared. Data for biol. activity of title compds. were given.

IT 393787-19-4P 393787-20-7P 393787-89-8P  
 393787-90-1P 393787-91-2P 393787-92-3P  
 393788-00-6P 393788-02-8P 393788-04-0P  
 393788-18-6P 393788-20-0P 393788-27-7P  
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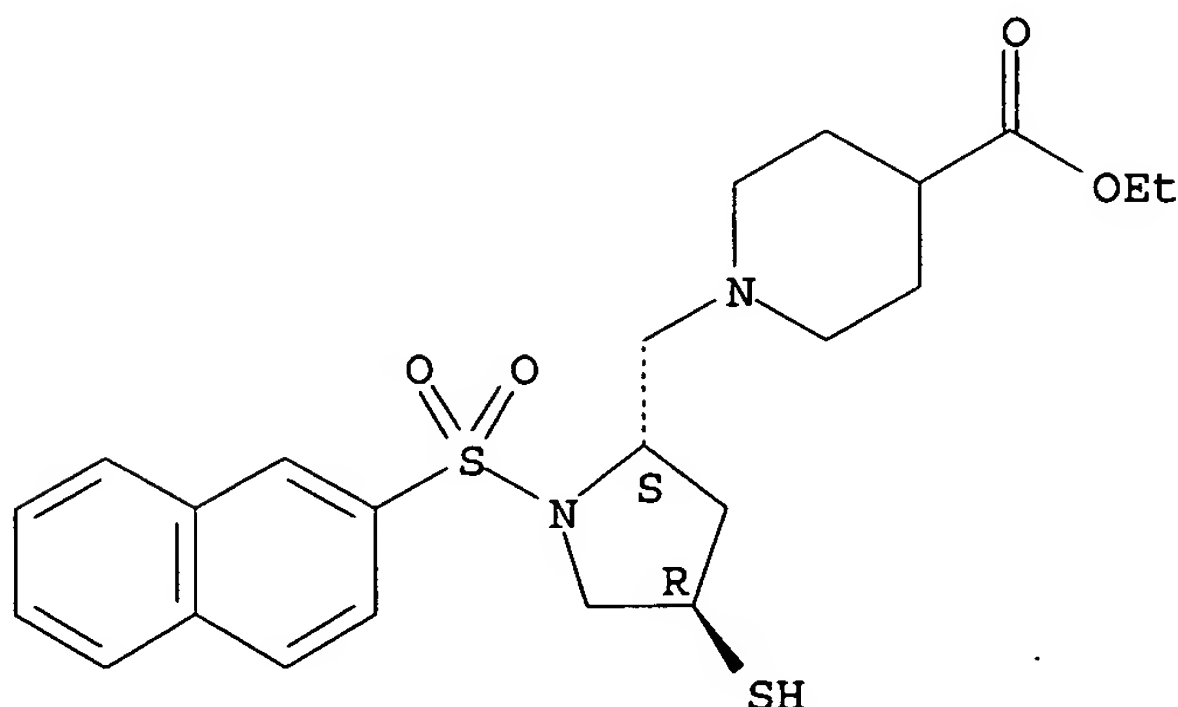
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrrolidinethiols and analogs as metalloprotease inhibitors)

RN 393787-19-4 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

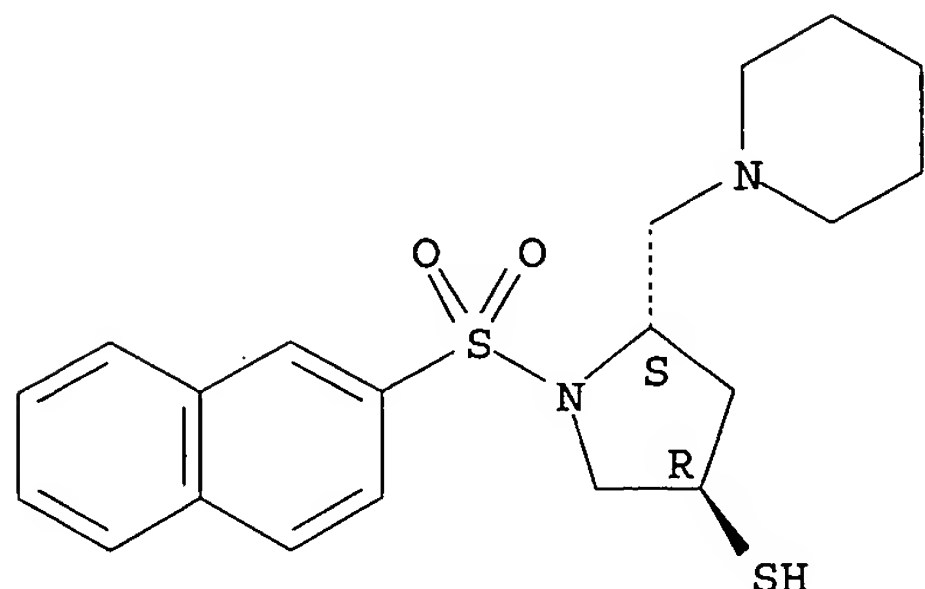
Absolute stereochemistry.



RN 393787-20-7 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-(1-piperidinylmethyl)-,  
(3R,5S)- (9CI) (CA INDEX NAME)

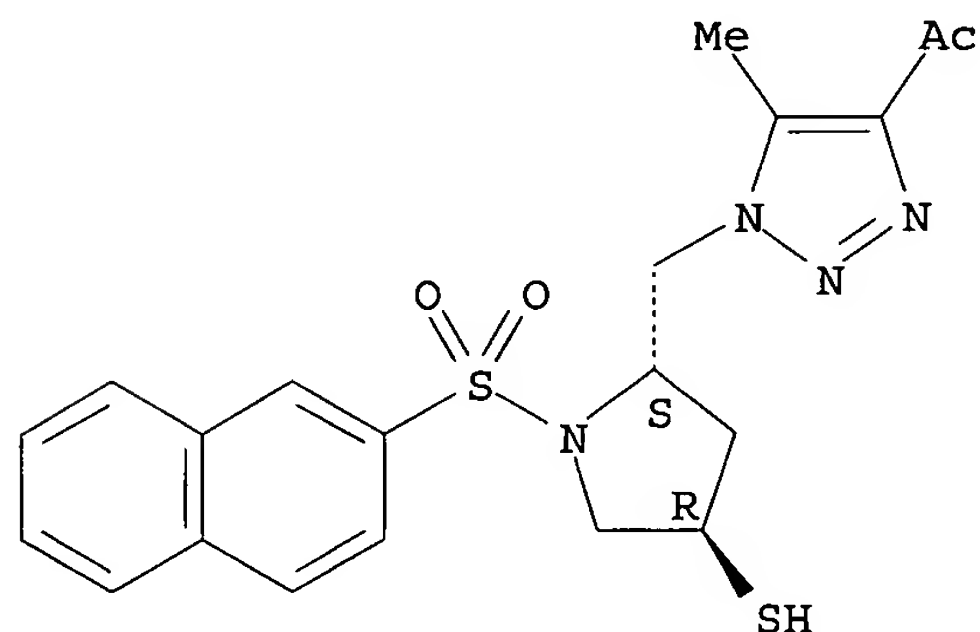
Absolute stereochemistry.



RN 393787-89-8 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(4-acetyl-5-methyl-1H-1,2,3-triazol-1-yl)methyl]-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

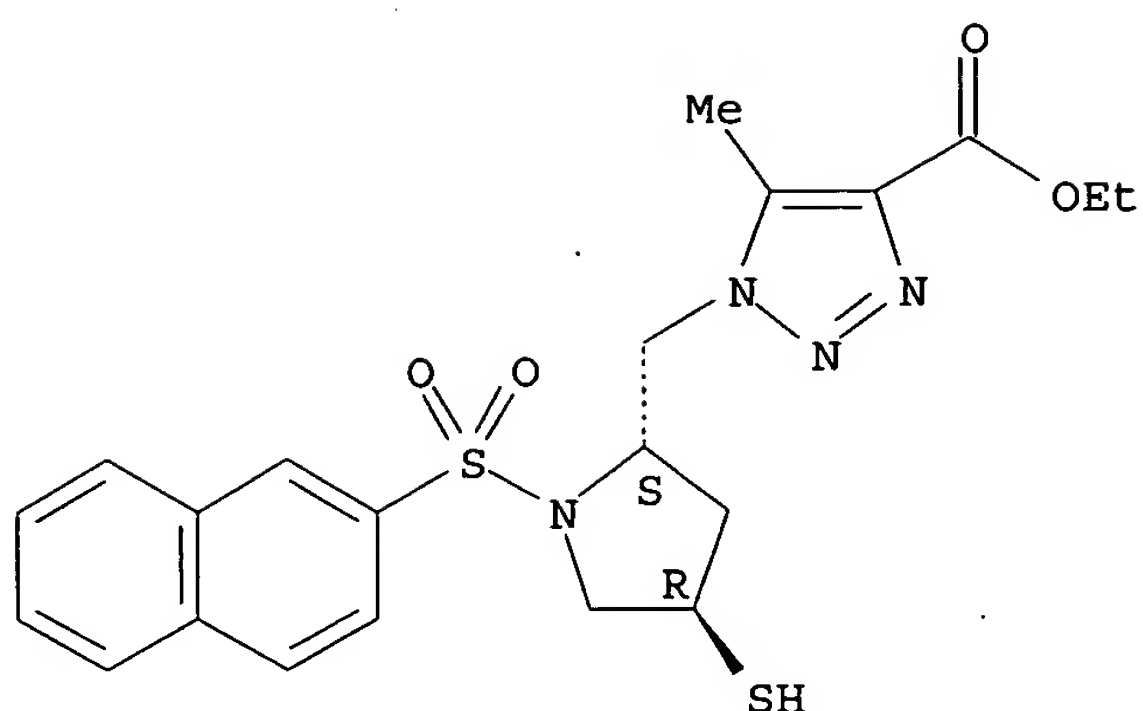
Absolute stereochemistry.



RN 393787-90-1 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxylic acid, 1-[[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]-5-methyl-, ethyl ester (9CI)  
(CA INDEX NAME)

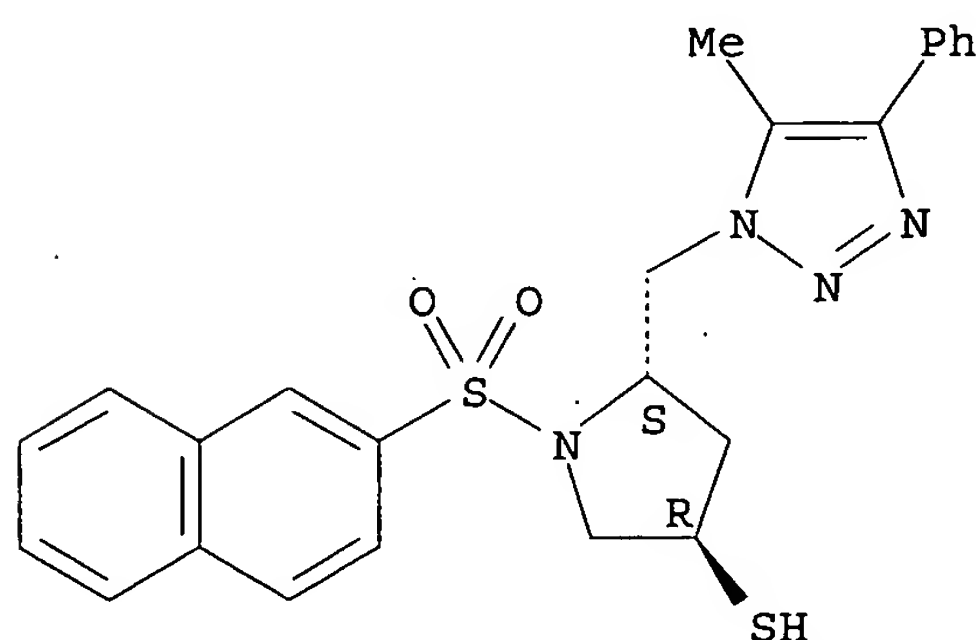
Absolute stereochemistry.



RN 393787-91-2 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(5-methyl-4-phenyl-1H-1,2,3-triazol-1-yl)methyl]-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

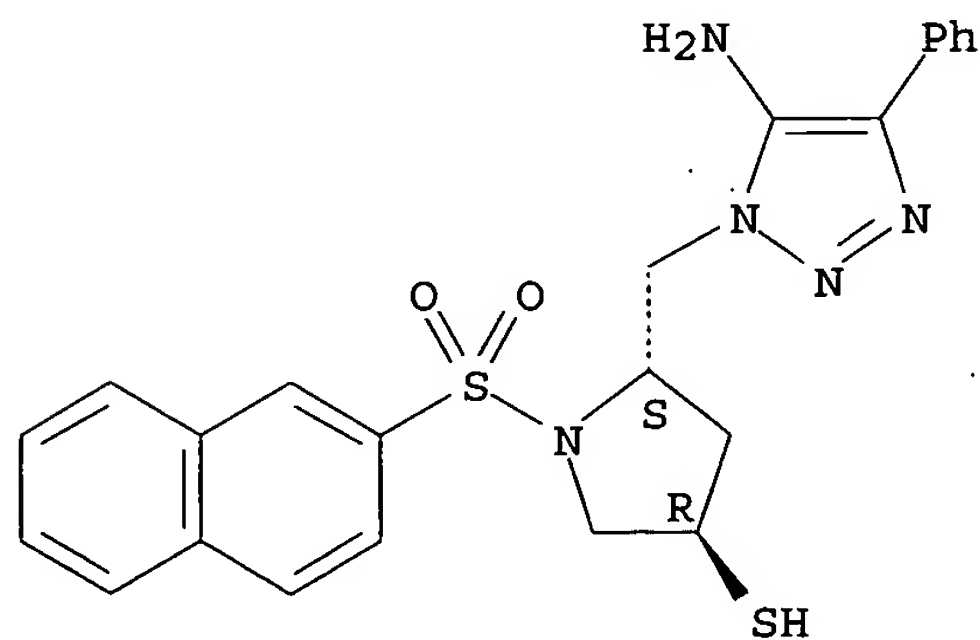
Absolute stereochemistry.



RN 393787-92-3 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(5-amino-4-phenyl-1H-1,2,3-triazol-1-yl)methyl]-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

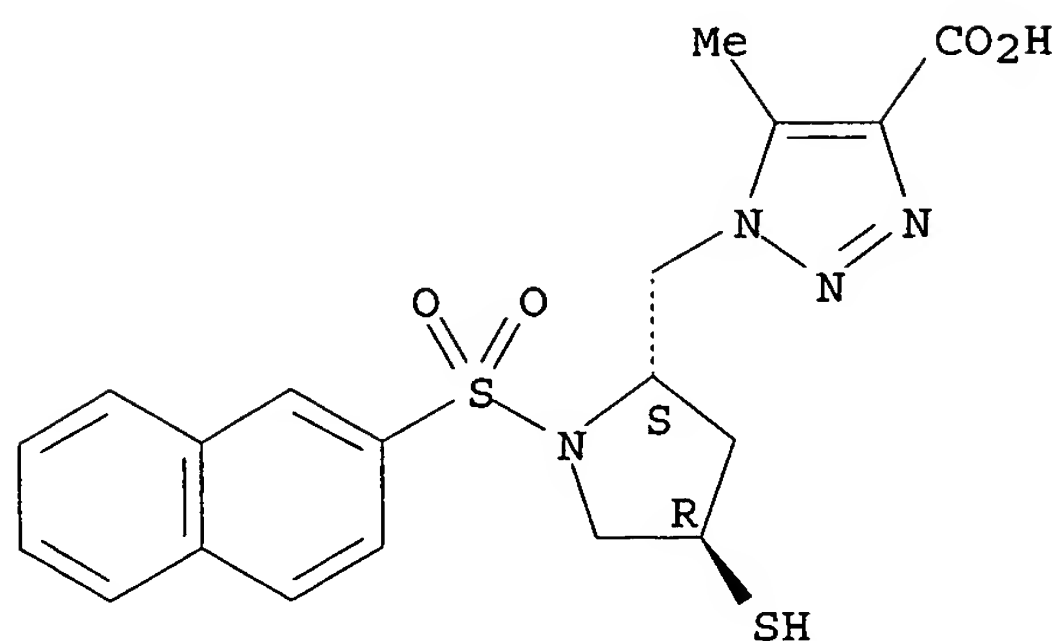


RN 393788-00-6 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxylic acid, 1-[[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]-5-methyl]- (9CI) (CA INDEX NAME)

NAME)

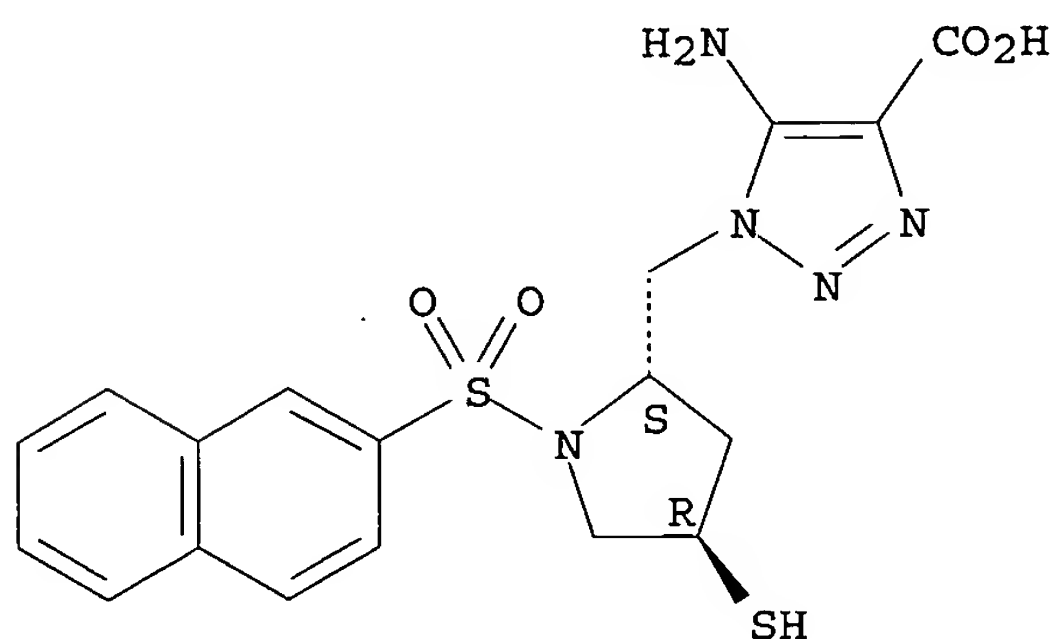
Absolute stereochemistry.



RN 393788-02-8 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxylic acid, 5-amino-1-[[2-(2-naphthalenylsulfonyl)-4-mercapto-1-pyrrolidinyl]methyl]- (9CI) (CA INDEX NAME)

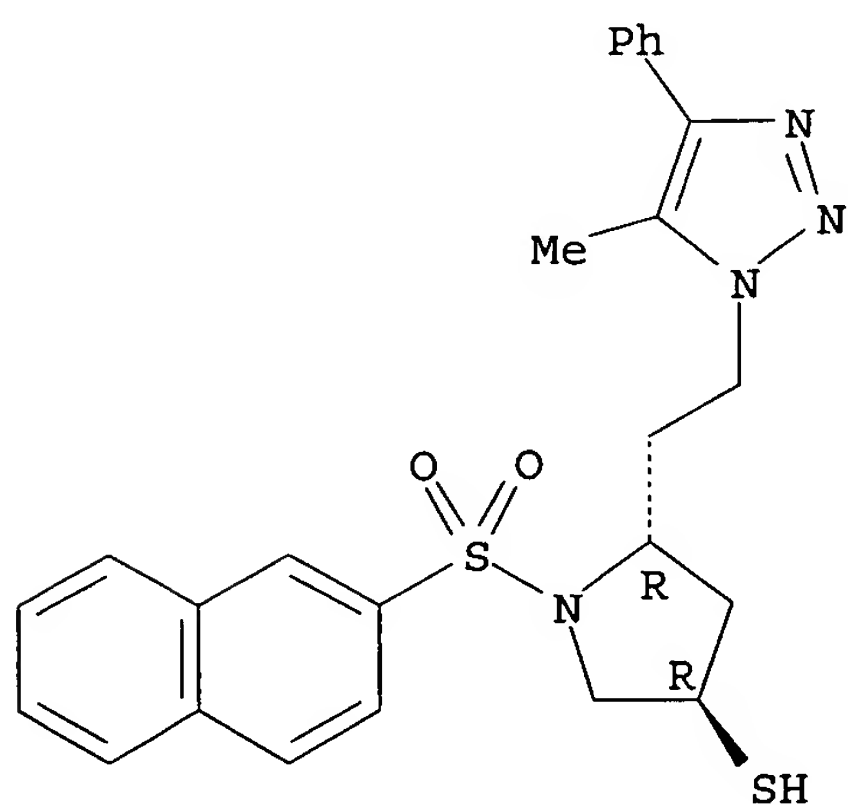
Absolute stereochemistry.



RN 393788-04-0 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[2-(5-methyl-4-phenyl-1H-1,2,3-triazol-1-yl)ethyl]-1-(2-naphthalenylsulfonyl)-, (3R,5R)- (9CI) (CA INDEX NAME)

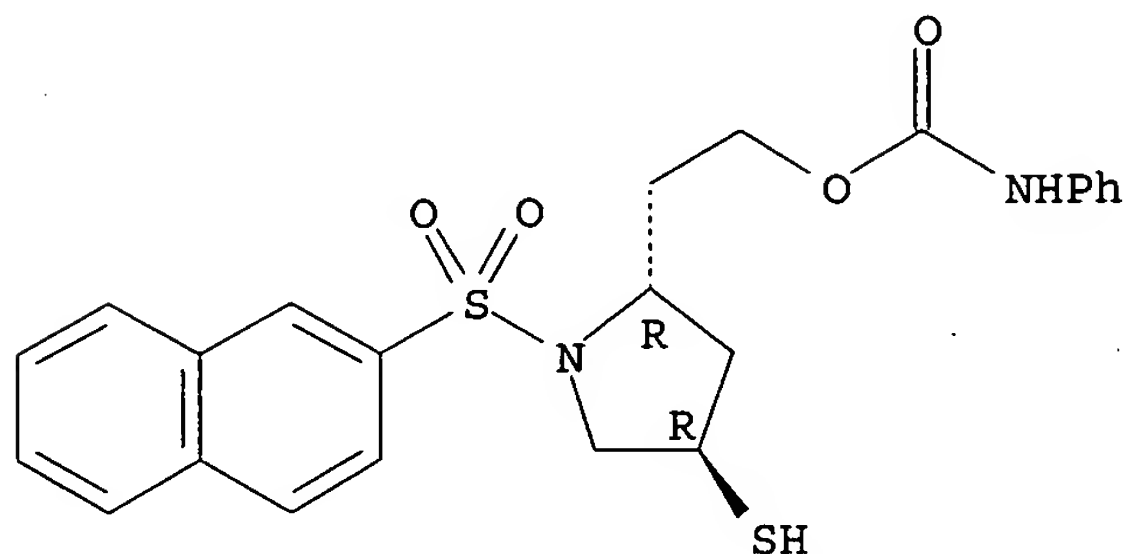
Absolute stereochemistry.



RN 393788-18-6 HCAPLUS

CN 2-Pyrrolidineethanol, 4-mercapto-1-(2-naphthalenylsulfonyl)-,  
α-(phenylcarbamate), (2R,4R)- (9CI) (CA INDEX NAME)

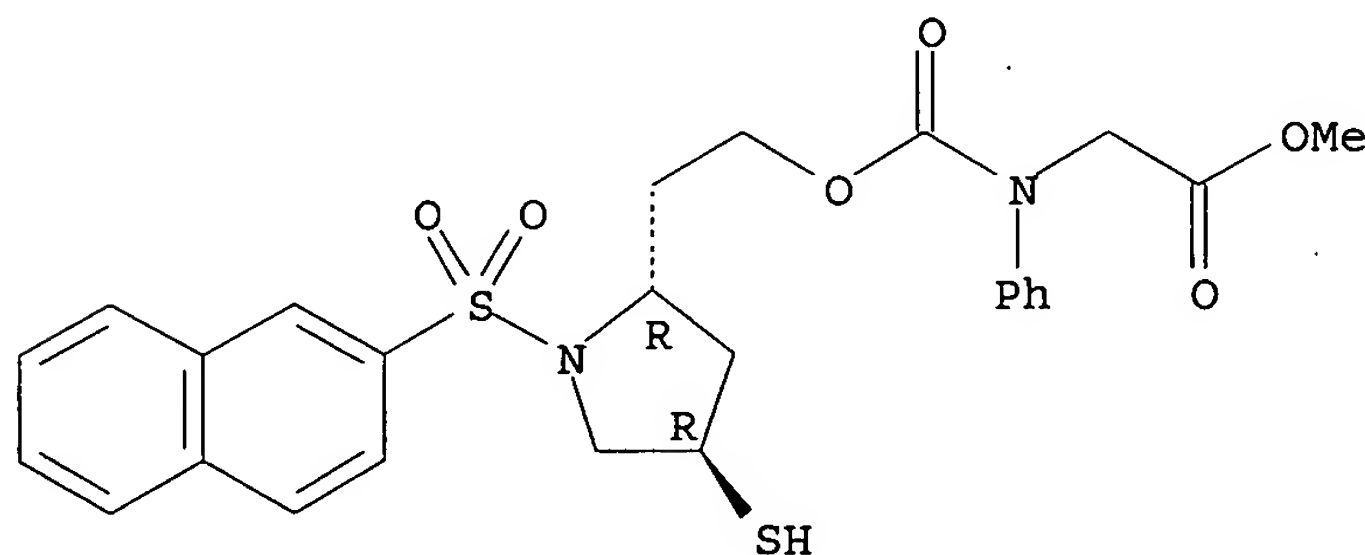
Absolute stereochemistry.



RN 393788-20-0 HCAPLUS

CN Glycine, N-[[2-[(2R,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]ethoxy]carbonyl]-N-phenyl-, methyl ester (9CI) (CA INDEX NAME)

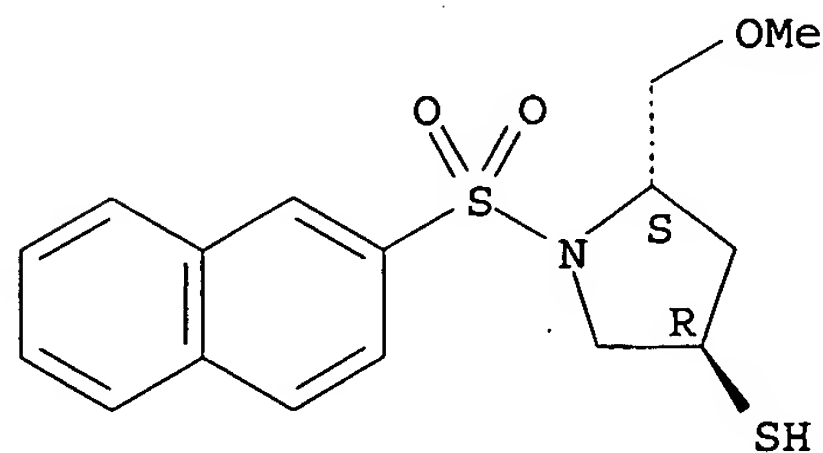
Absolute stereochemistry.



RN 393788-27-7 HCAPLUS

CN 3-Pyrrolidinethiol, 5-(methoxymethyl)-1-(2-naphthalenylsulfonyl)-,  
(3R,5S)- (9CI) (CA INDEX NAME)

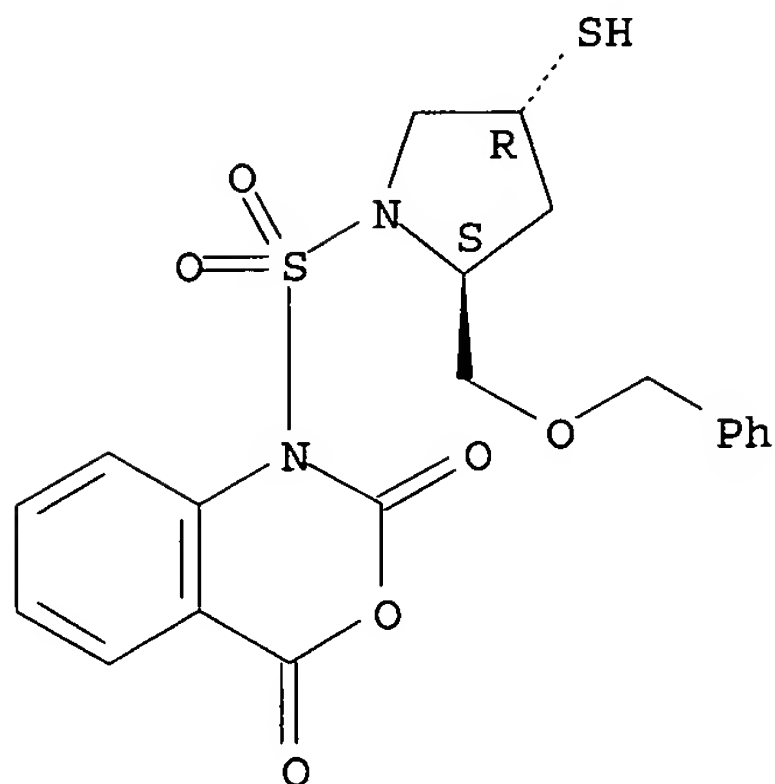
Absolute stereochemistry.



RN 393790-15-3 HCAPLUS

CN 2H-3,1-Benzoxazine-2,4(1H)-dione, 1-[[[(2S,4R)-4-mercapto-2-[(phenylmethoxy)methyl]-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

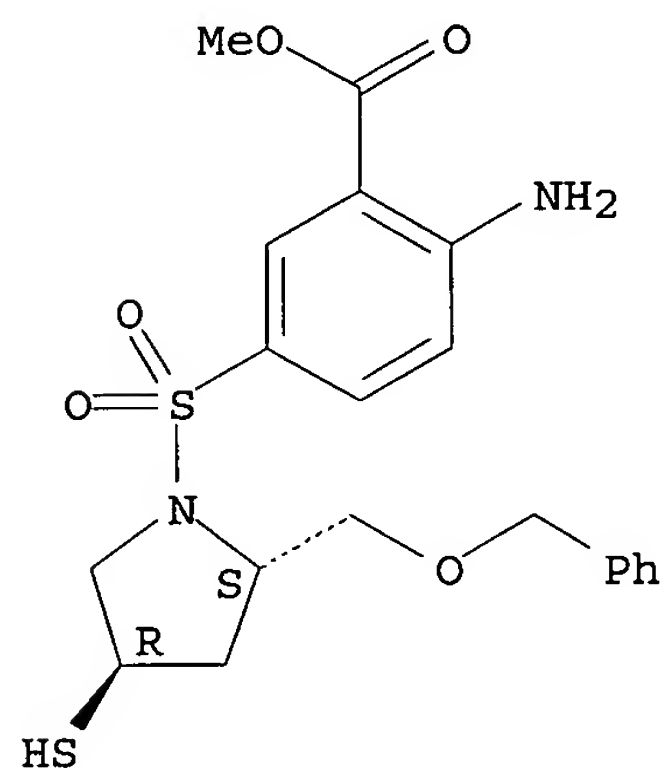
Absolute stereochemistry.



RN 393790-17-5 HCAPLUS

CN Benzoic acid, 2-amino-5-[[[(2S,4R)-4-mercapto-2-[(phenylmethoxy)methyl]-1-pyrrolidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

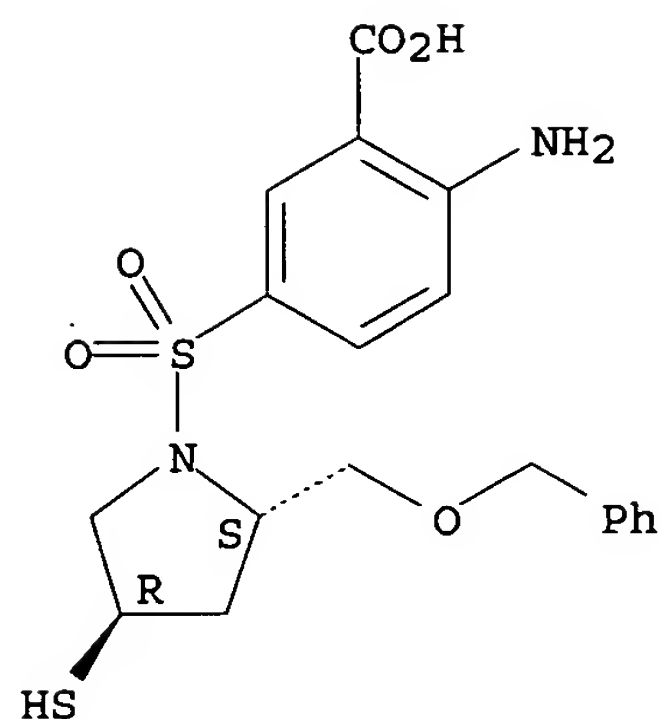


RN 393790-19-7 HCAPLUS

CN Benzoic acid, 2-amino-5-[[[(2S,4R)-4-mercapto-2-[(phenylmethoxy)methyl]-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

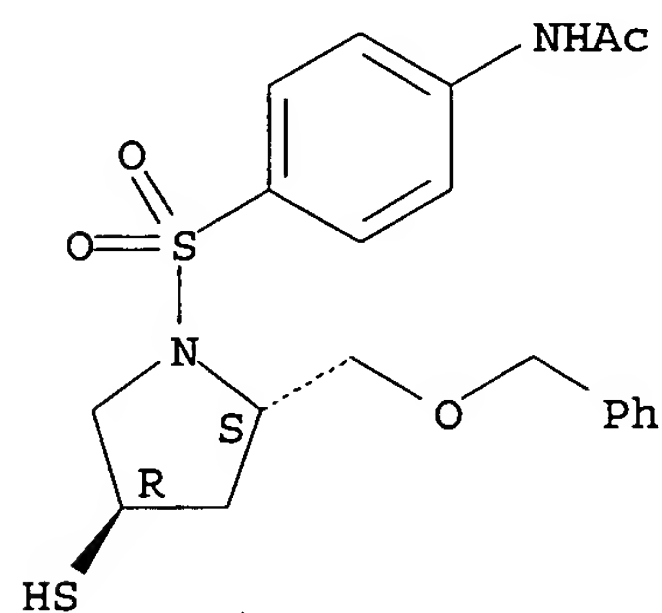




RN 393790-20-0 HCAPLUS

CN Acetamide, N-[4-[[[(2S,4R)-4-mercapto-2-[(phenylmethoxy)methyl]-1-pyrrolidinyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

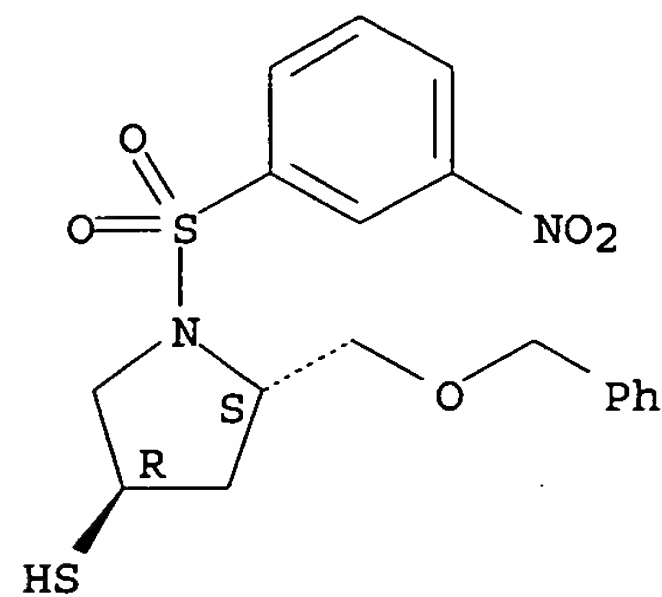
Absolute stereochemistry.



RN 393790-21-1 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(3-nitrophenyl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

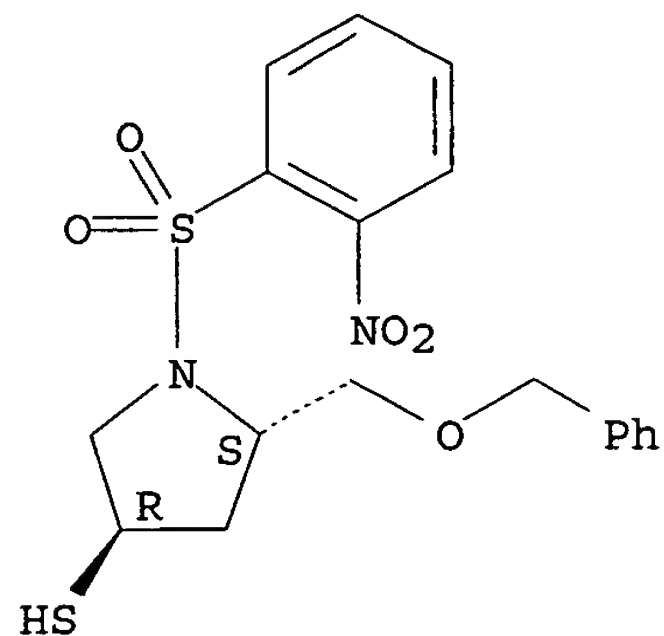
Absolute stereochemistry.



RN 393790-22-2 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(2-nitrophenyl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

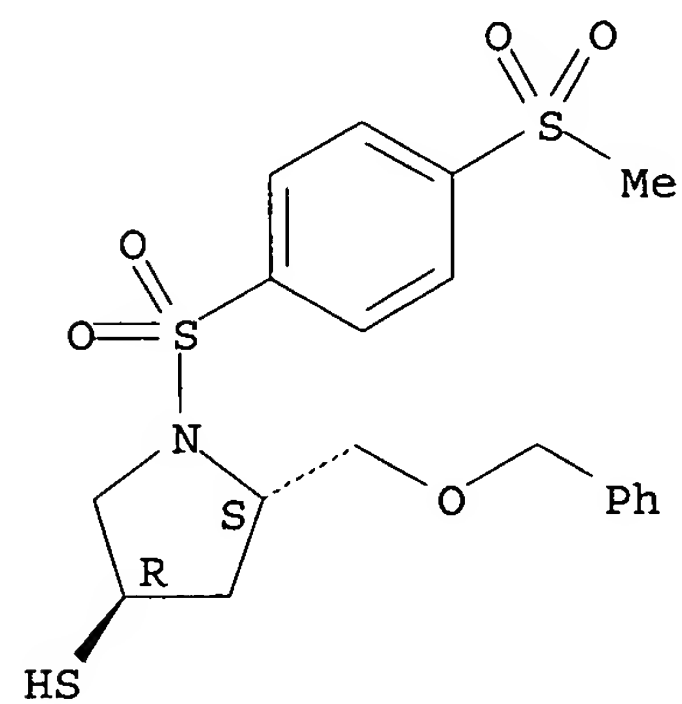
Absolute stereochemistry.



RN 393790-23-3 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[[4-(methylsulfonyl)phenyl]sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

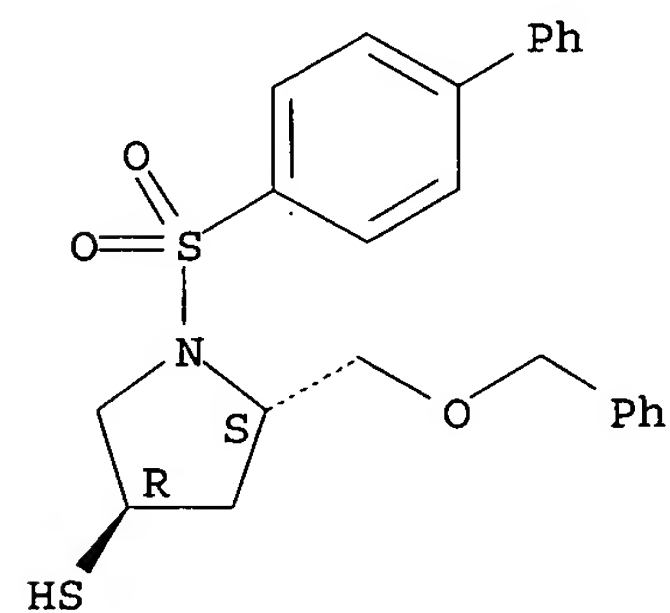
Absolute stereochemistry.



RN 393790-24-4 HCAPLUS

CN 3-Pyrrolidinethiol, 1-([1,1'-biphenyl]-4-ylsulfonyl)-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

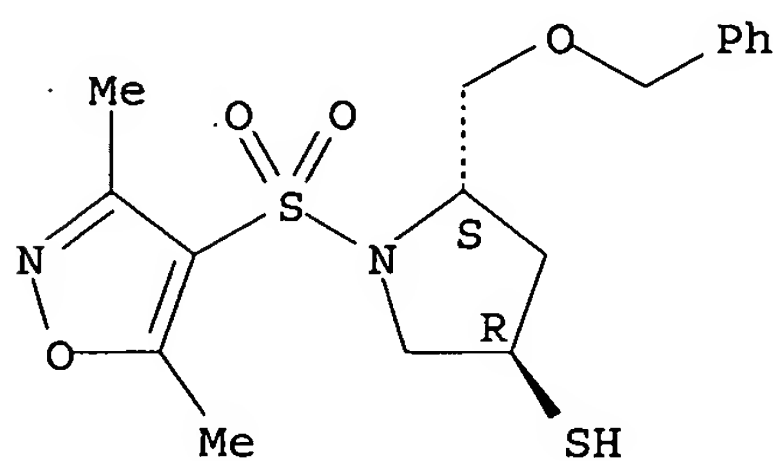


RN 393790-26-6 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

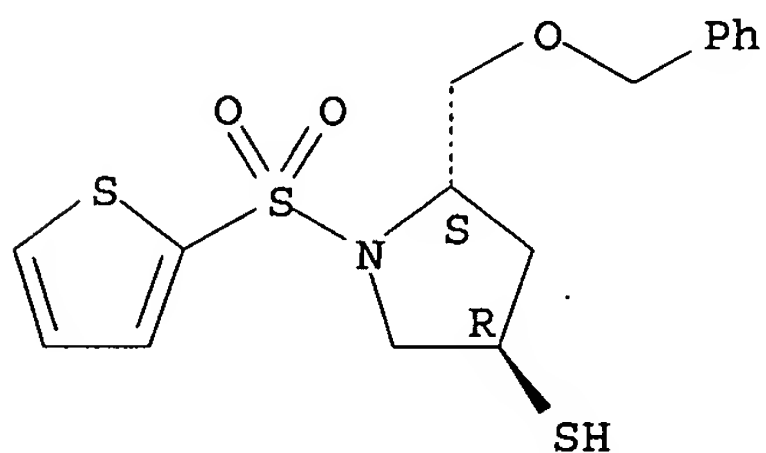
Absolute stereochemistry.



RN 393790-27-7 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(phenylmethoxy)methyl]-1-(2-thienylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

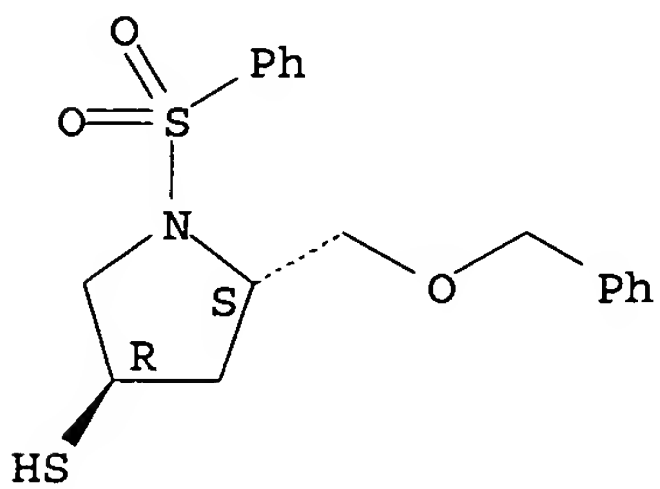
Absolute stereochemistry.



RN 393790-28-8 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(phenylmethoxy)methyl]-1-(phenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

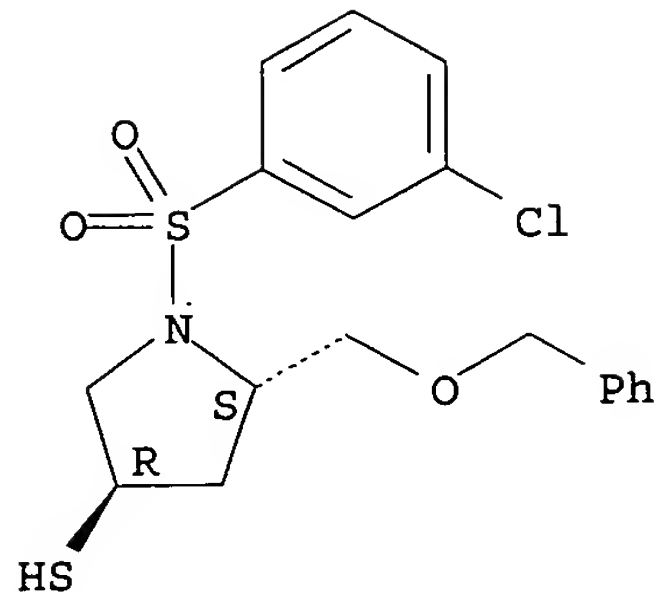
Absolute stereochemistry.



RN 393790-29-9 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(3-chlorophenyl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

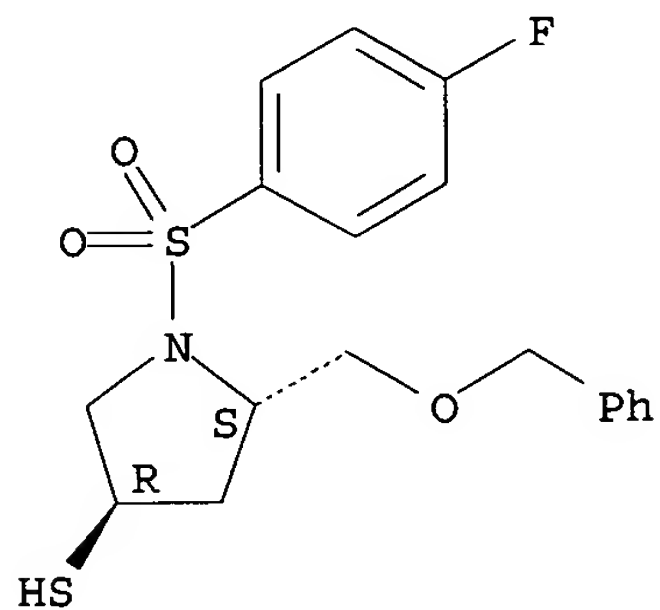
Absolute stereochemistry.



RN 393790-32-4 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(4-fluorophenyl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

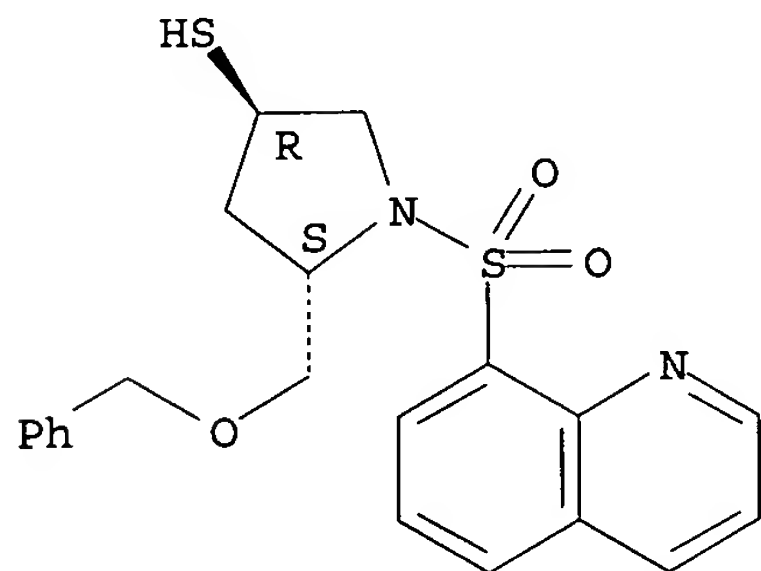
Absolute stereochemistry.



RN 393790-34-6 HCAPLUS

CN 3-Pyrrolidinethiol, 5-[(phenylmethoxy)methyl]-1-(8-quinolinylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

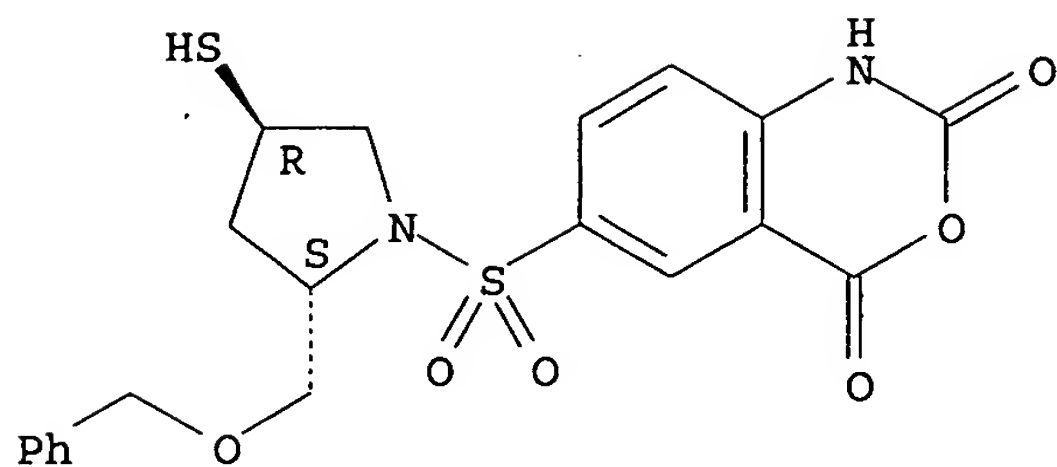
Absolute stereochemistry.



RN 393790-35-7 HCAPLUS

CN 3-Pyrrolidinethiol, 1-[(1,4-dihydro-2,4-dioxo-2H-3,1-benzoxazin-6-yl)sulfonyl]-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

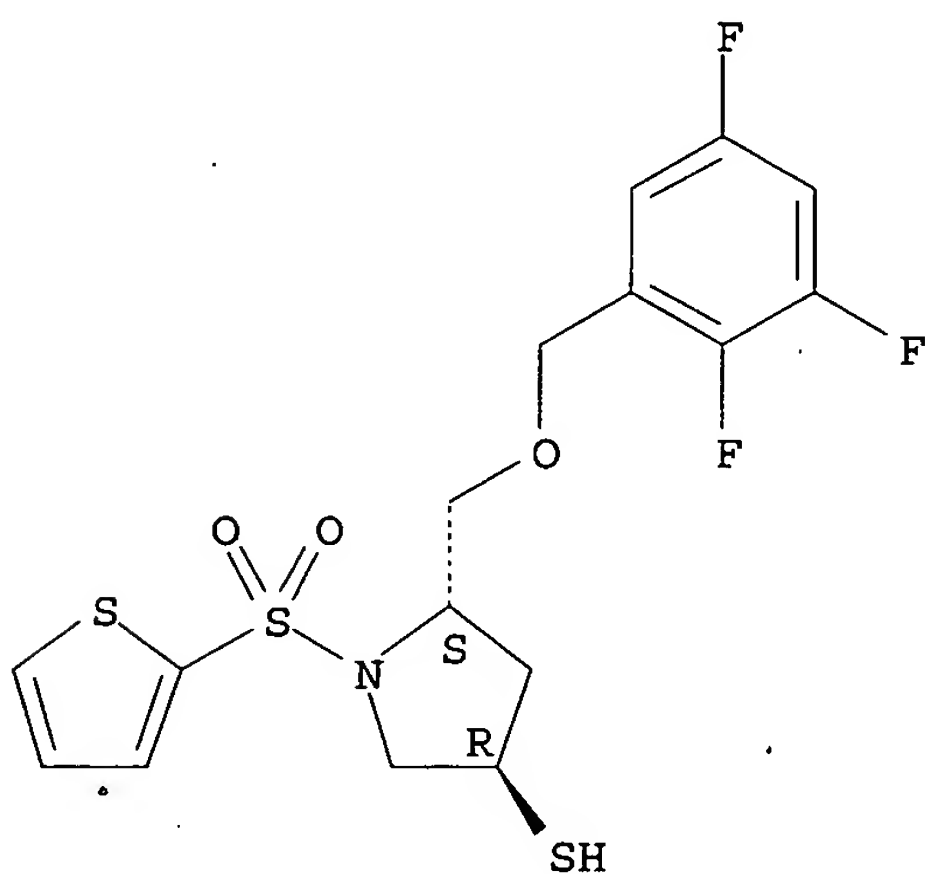
Absolute stereochemistry.



RN 393790-36-8 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-thienylsulfonyl)-5-[[2,3,5-trifluorophenyl)methoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

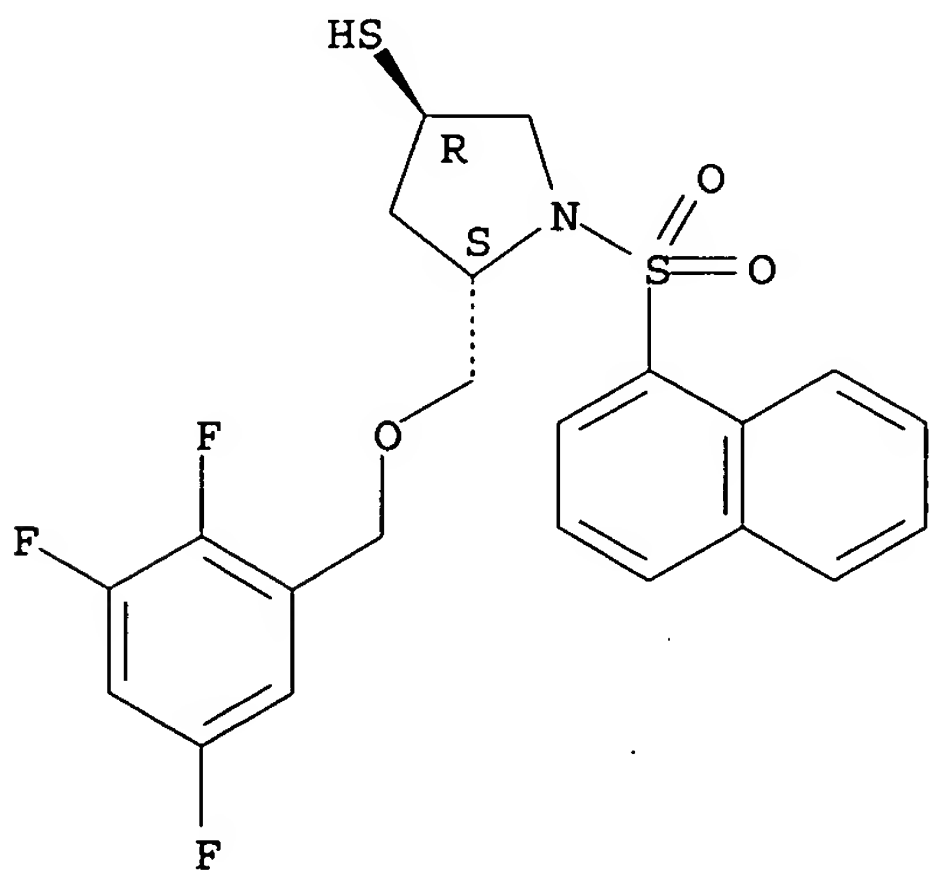
Absolute stereochemistry.



RN 393790-39-1 HCAPLUS

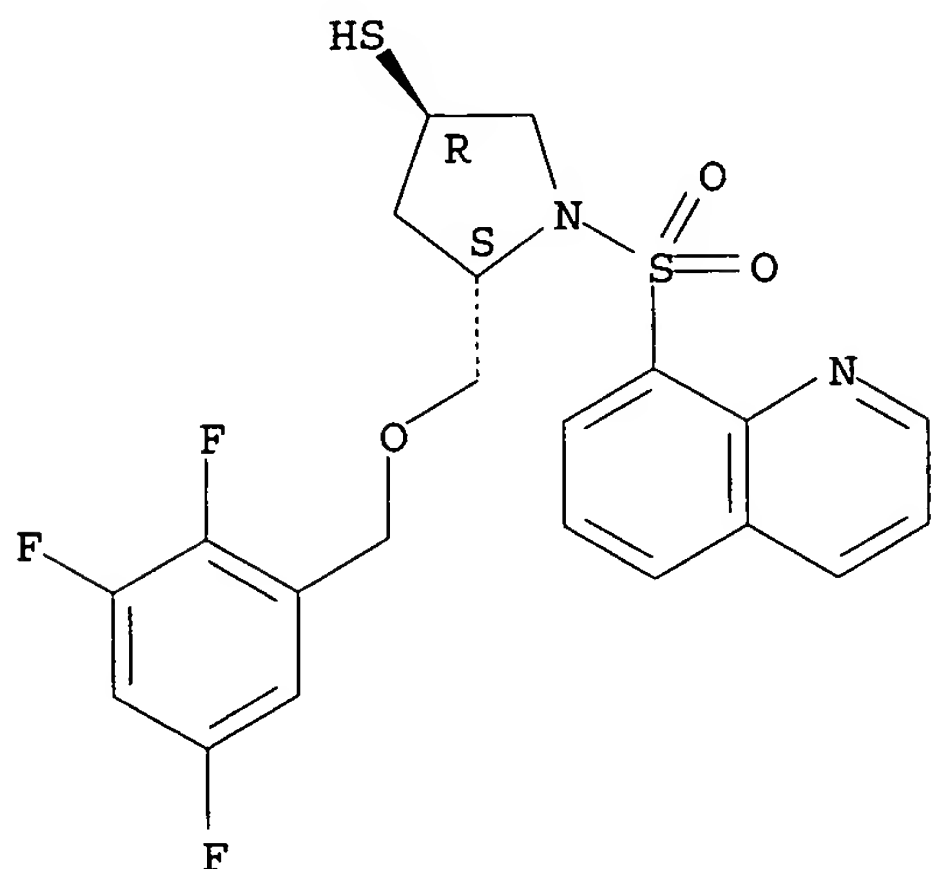
CN 3-Pyrrolidinethiol, 1-(1-naphthalenylsulfonyl)-5-[[2,3,5-trifluorophenyl)methoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



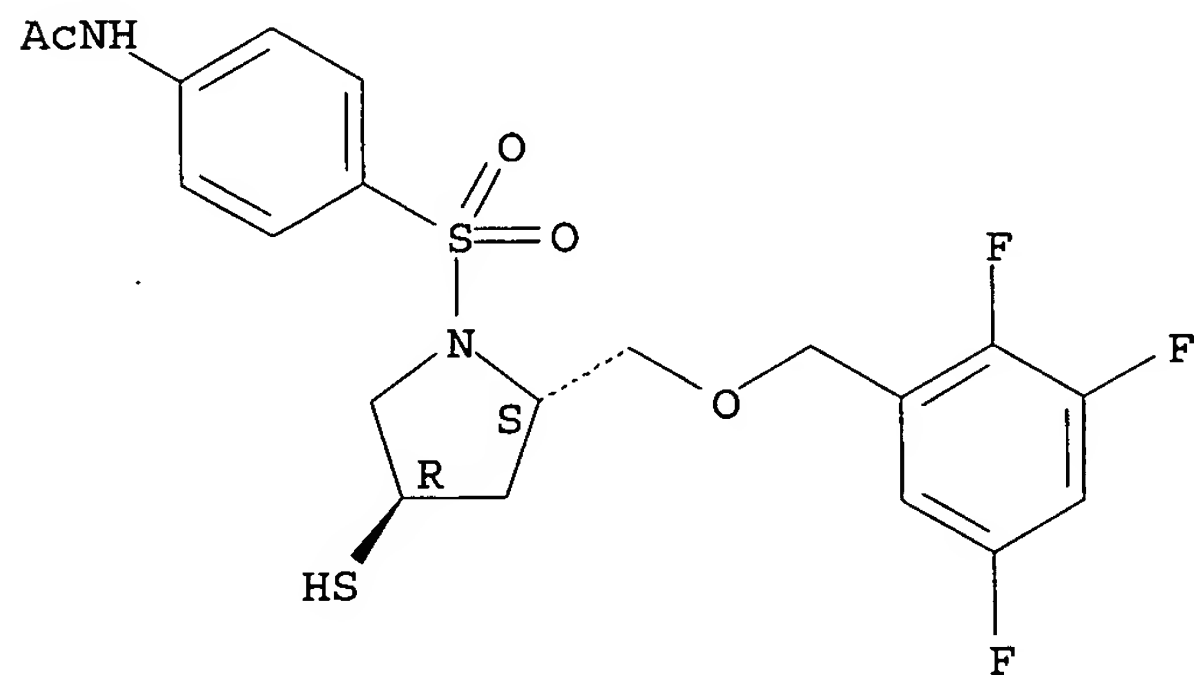
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 CN 3-Pyrrolidinethiol, 1-(8-quinolinylsulfonyl)-5-[[[(2,3,5-trifluorophenyl)methoxy]methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



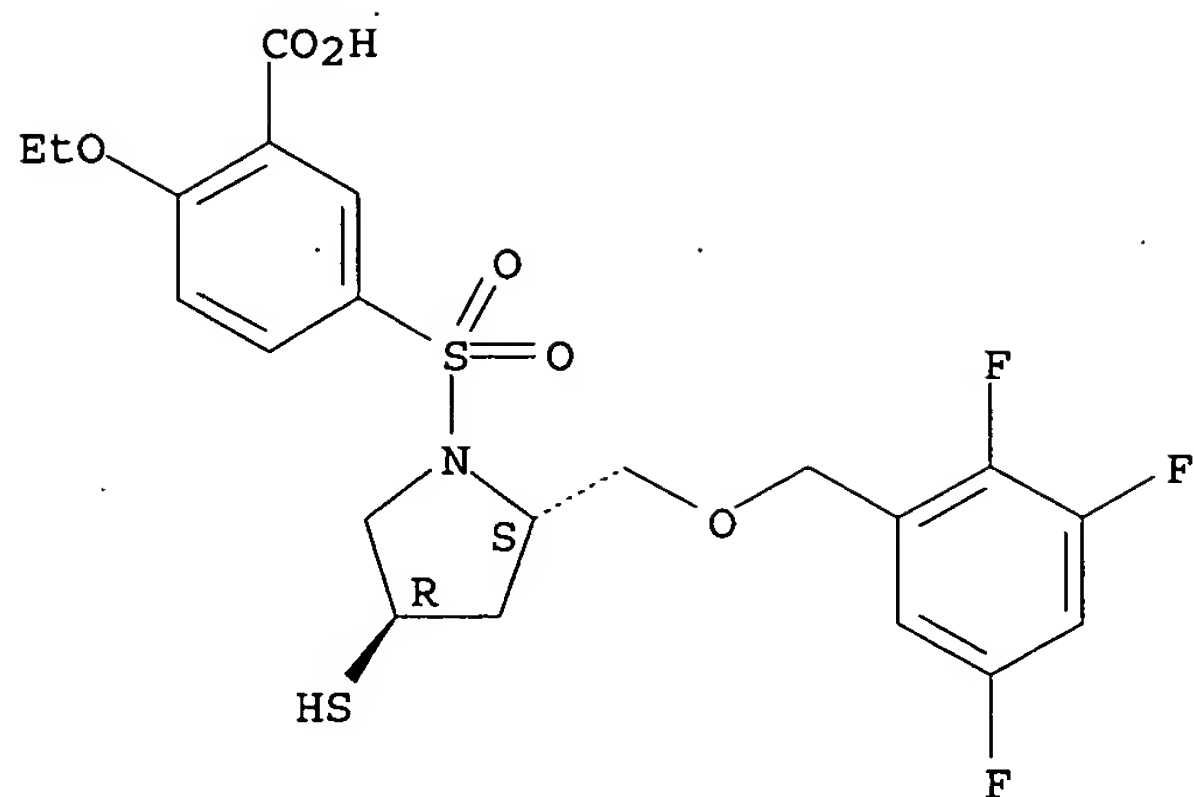
RN 393790-46-0 HCAPLUS  
 CN Acetamide, N-[4-[[[(2S,4R)-4-mercapto-2-[[[(2,3,5-trifluorophenyl)methoxy]methyl]-1-pyrrolidinyl]sulfonyl]phenyl]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



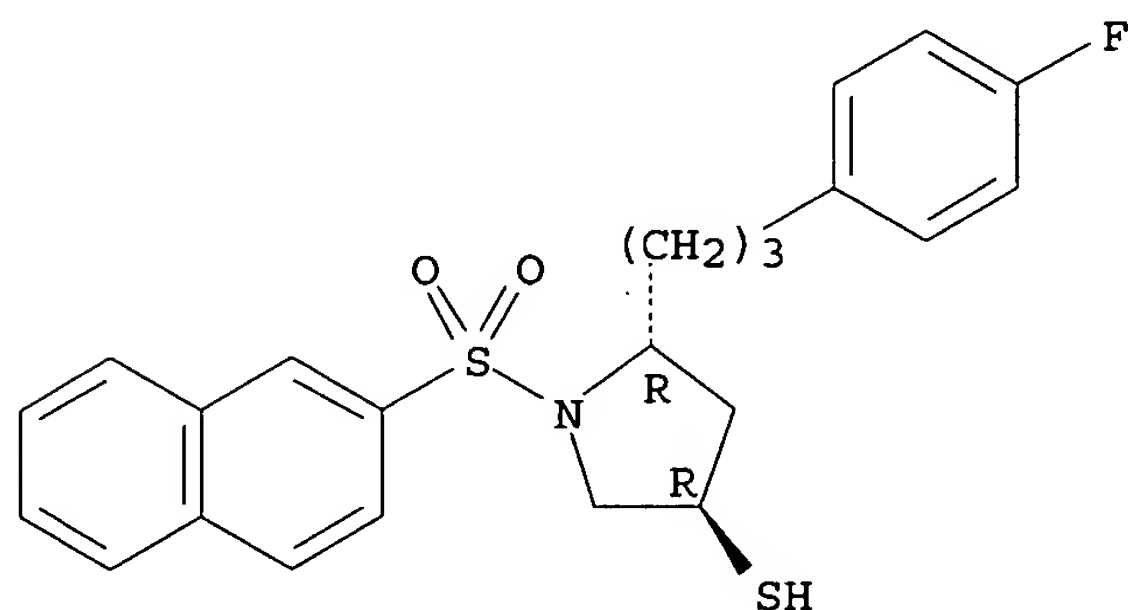
RN 393790-47-1 HCAPLUS  
 CN Benzoic acid, 2-ethoxy-5-[[[(2S,4R)-4-mercapto-2-[[[(2,3,5-trifluorophenyl)methoxy]methyl]-1-pyrrolidinyl]sulfonyl]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



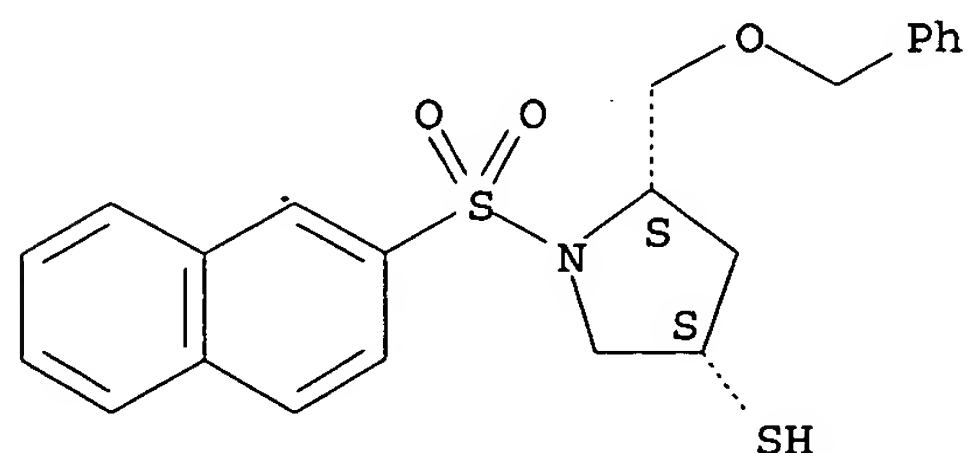
RN 393791-26-9 HCAPLUS  
 CN 3-Pyrrolidinethiol, 5-[3-(4-fluorophenyl)propyl]-1-(2-naphthalenylsulfonyl)-, (3R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



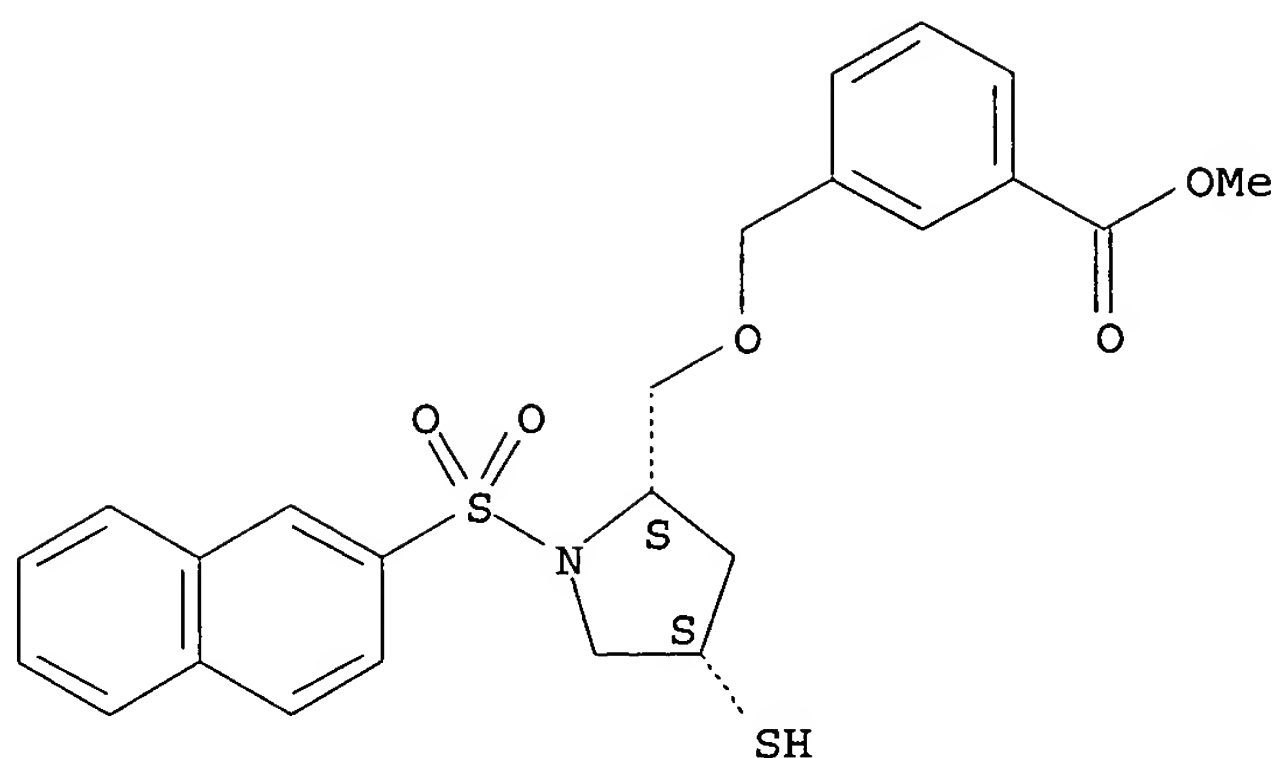
RN 393791-27-0 HCAPLUS  
 CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, (3S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393791-28-1 HCAPLUS  
 CN Benzoic acid, 3-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

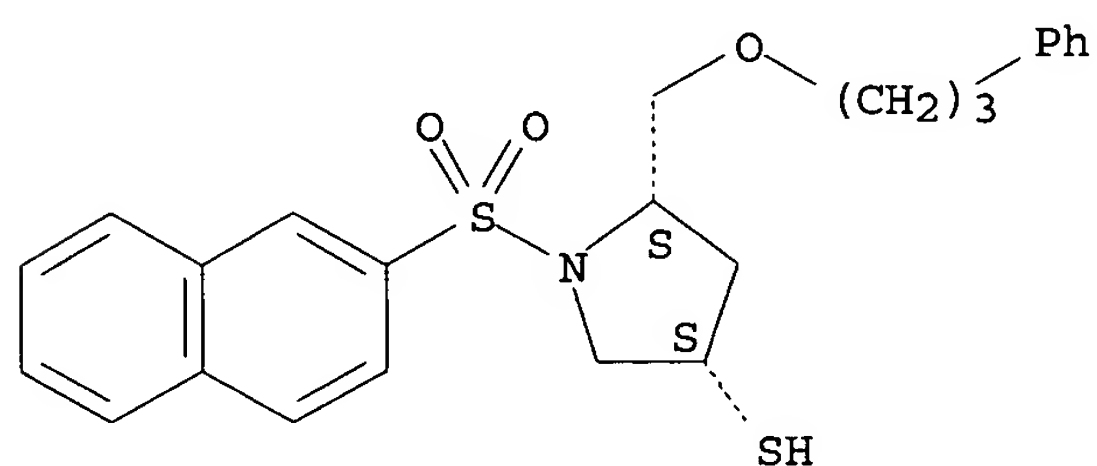
Absolute stereochemistry.



RN 393791-29-2 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-, (3S,5S)- (9CI) (CA INDEX NAME)

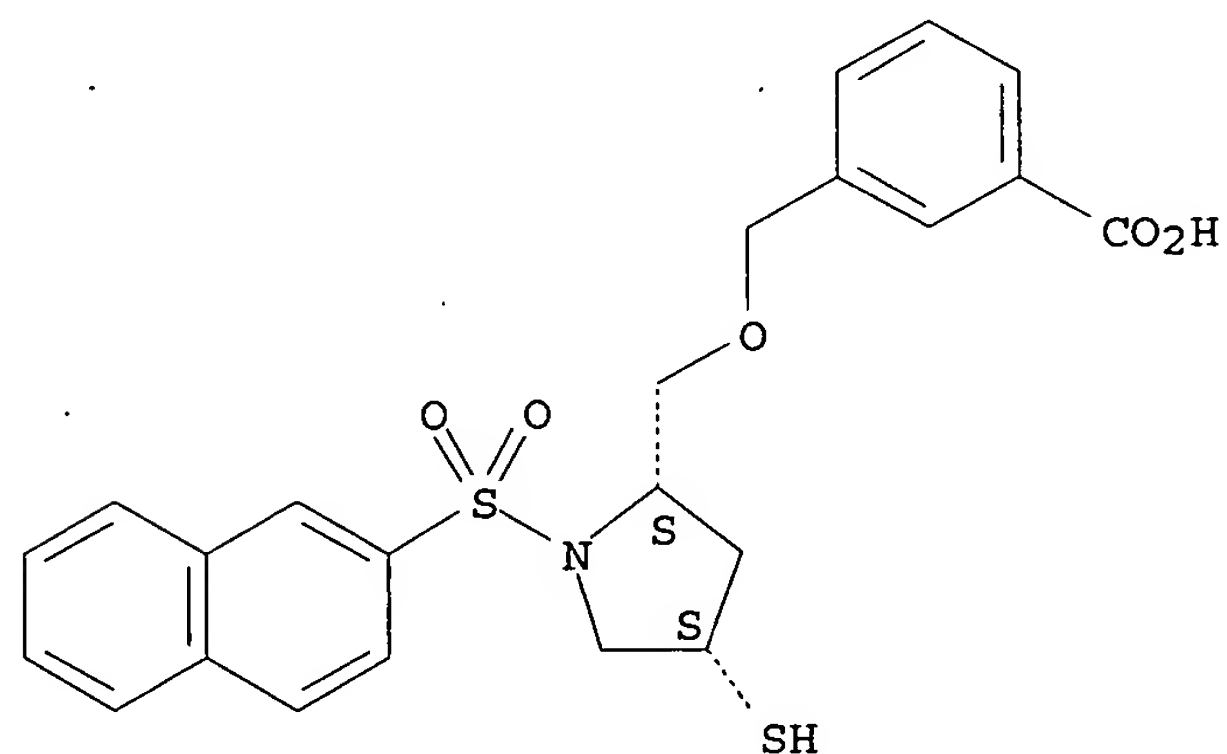
Absolute stereochemistry.



RN 393791-32-7 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



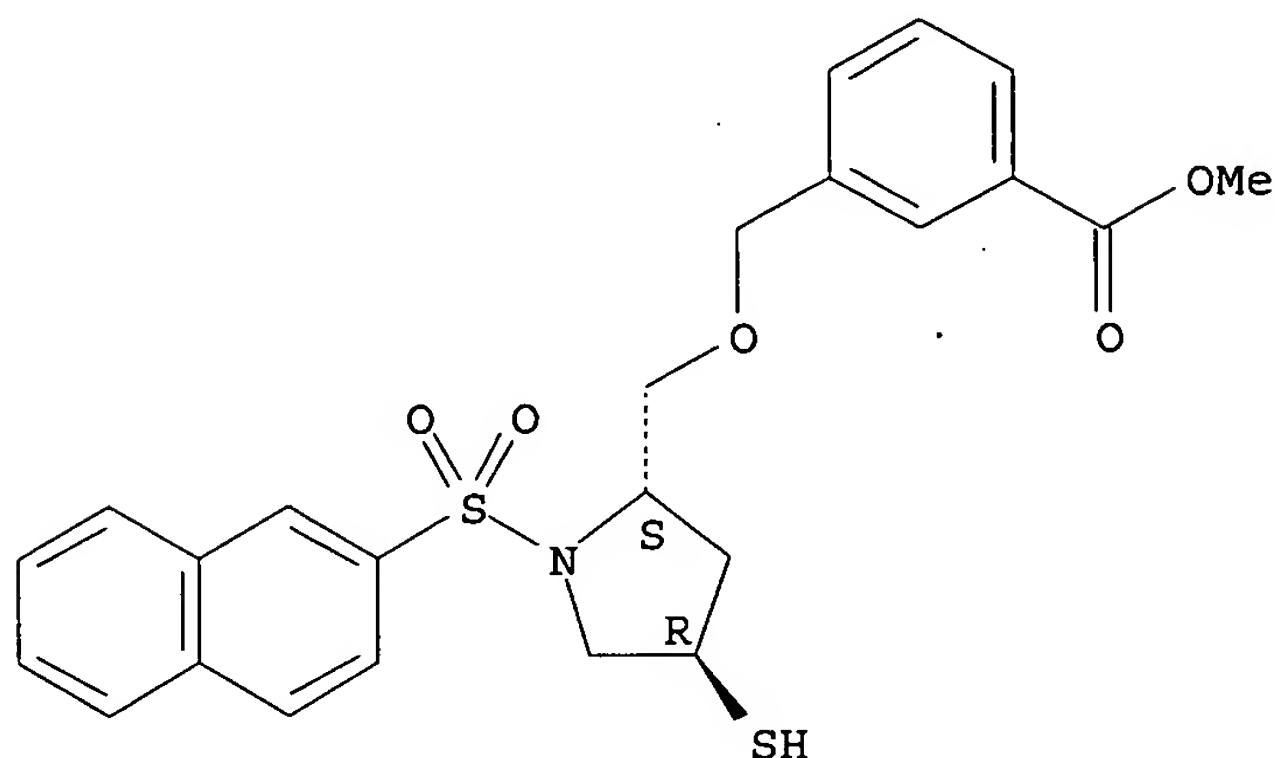
RN 393791-33-8 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-



pyrrolidinyl]methoxy)methyl]-, methyl ester (9CI) (CA INDEX NAME)

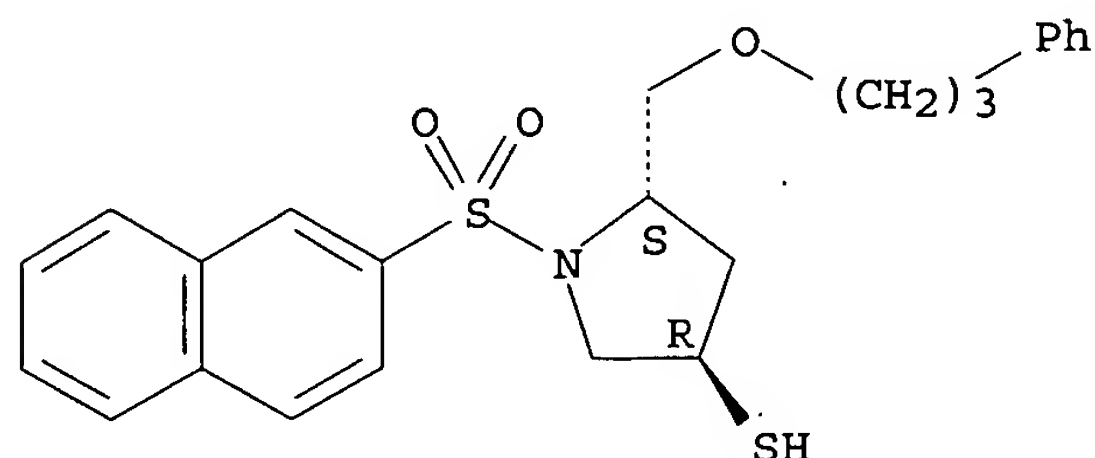
Absolute stereochemistry.



RN 393791-34-9 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

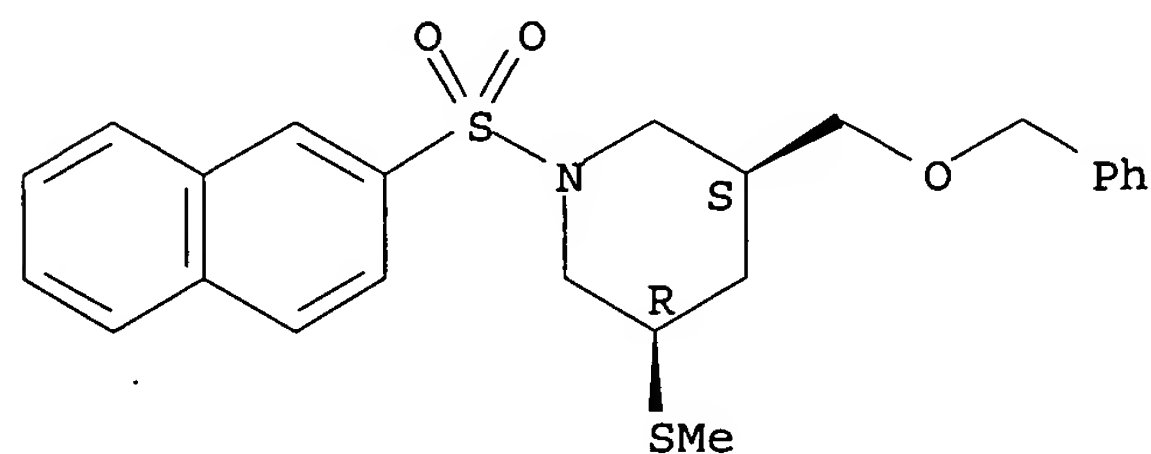
Absolute stereochemistry.



RN 393791-36-1 HCAPLUS

CN Piperidine, 3-(methylthio)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, (3R,5S)-rel- (9CI) (CA INDEX NAME)

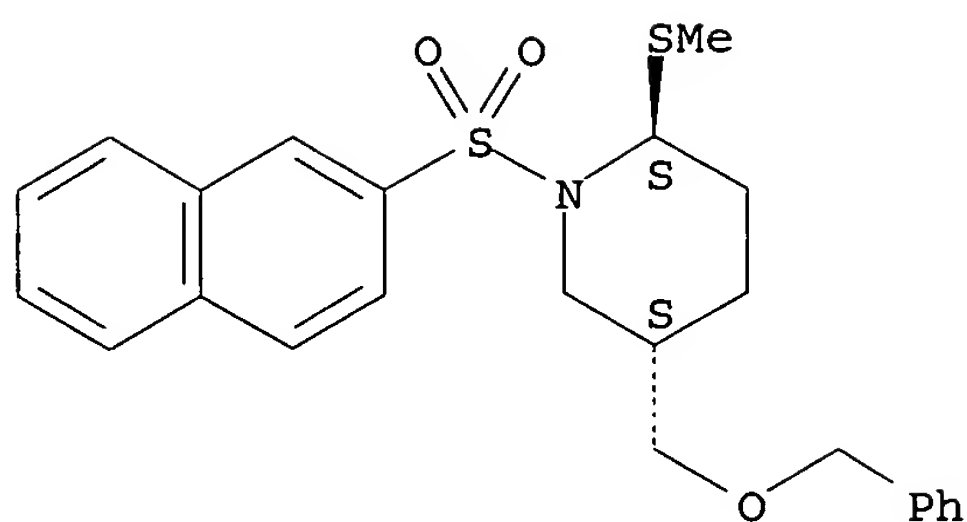
Relative stereochemistry.



RN 393791-37-2 HCAPLUS

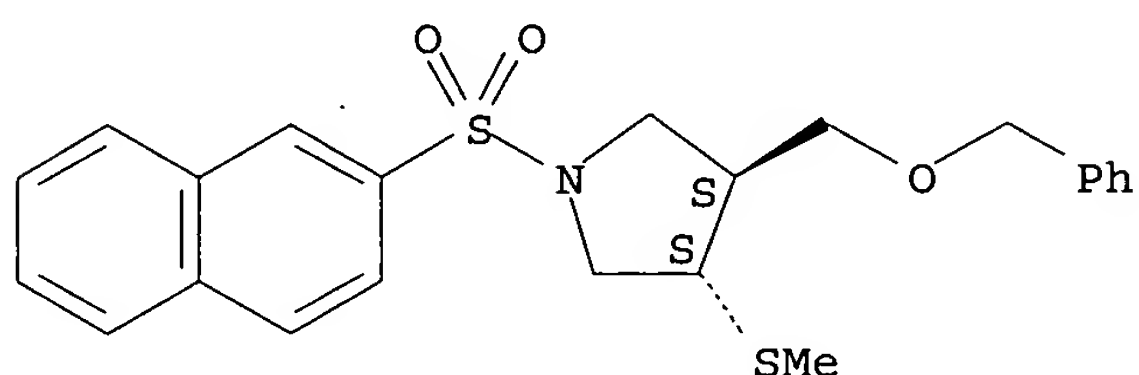
CN Piperidine, 2-(methylthio)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



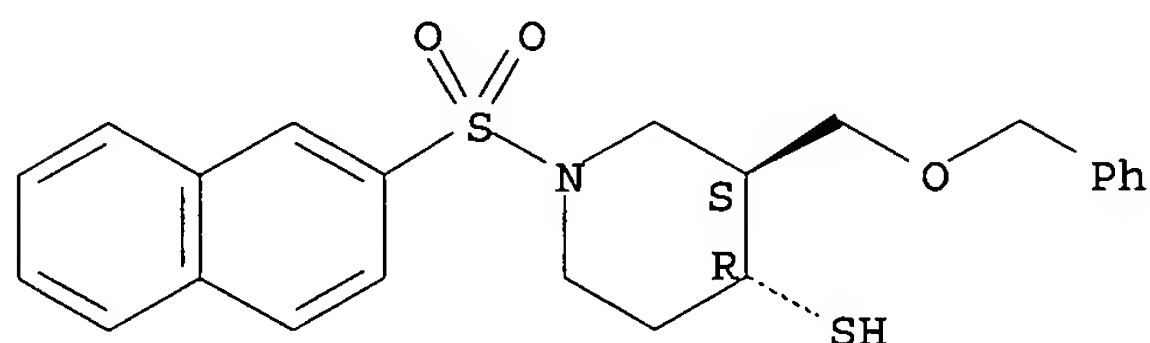
RN 393791-42-9 HCAPLUS  
 CN Pyrrolidine, 3-(methylthio)-1-(2-naphthalenylsulfonyl)-4-  
 [(phenylmethoxy)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



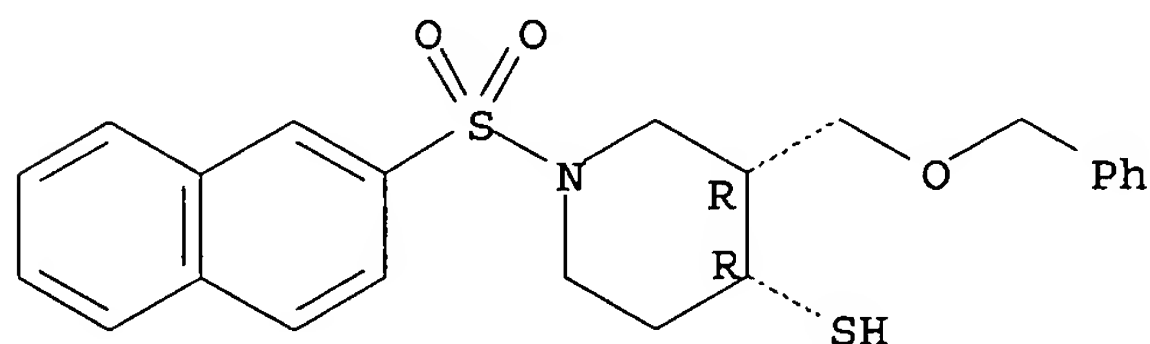
RN 393791-43-0 HCAPLUS  
 CN 4-Piperidinethiol, 1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-,  
 (3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 393791-44-1 HCAPLUS  
 CN 4-Piperidinethiol, 1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-,  
 (3R,4R)-rel- (9CI) (CA INDEX NAME)

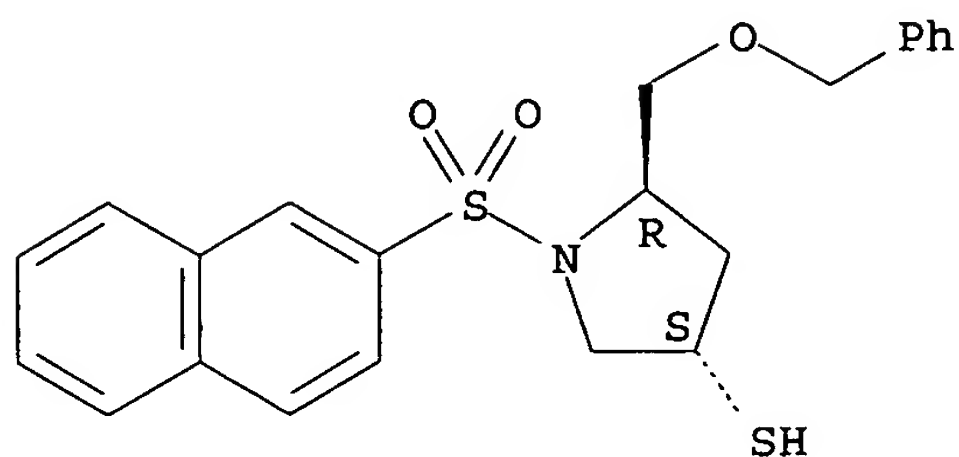
Relative stereochemistry.



RN 393793-31-2 HCAPLUS  
 CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-,

(3S,5R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 393793-82-3

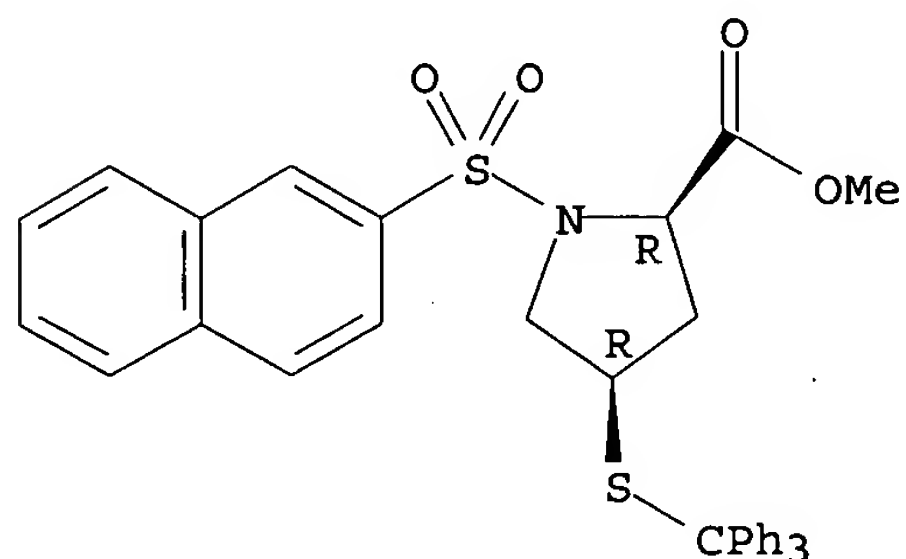
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyrrolidinethiols and analogs as metalloprotease inhibitors)

RN 393793-82-3 HCAPLUS

CN D-Proline, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl ester, (4R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 391671-83-3P 391671-85-5P 391671-90-2P  
 391671-92-4P 391672-17-6P 391672-19-8P  
 393153-99-6P 393792-17-1P 393792-19-3P  
 393792-20-6P 393792-21-7P 393792-22-8P  
 393792-26-2P 393792-27-3P 393792-28-4P  
 393792-63-7P 393793-01-6P 393793-02-7P  
 393793-06-1P 393793-07-2P 393793-08-3P  
 393793-09-4P 393793-13-0P 393793-14-1P  
 393793-15-2P 393793-18-5P 393793-19-6P  
 393793-20-9P 393793-23-2P 393793-24-3P  
 393793-25-4P 393793-27-6P 393793-28-7P  
 393793-29-8P 393793-33-4P 393793-34-5P  
 393793-36-7P 393793-37-8P 393793-39-0P  
 393793-40-3P 393793-41-4P 393793-42-5P  
 393793-44-7P 393793-45-8P 393793-47-0P  
 393793-48-1P 393793-51-6P 393793-60-7P  
 393793-61-8P 393793-63-0P 393793-64-1P  
 393793-65-2P 393793-69-6P 393793-70-9P

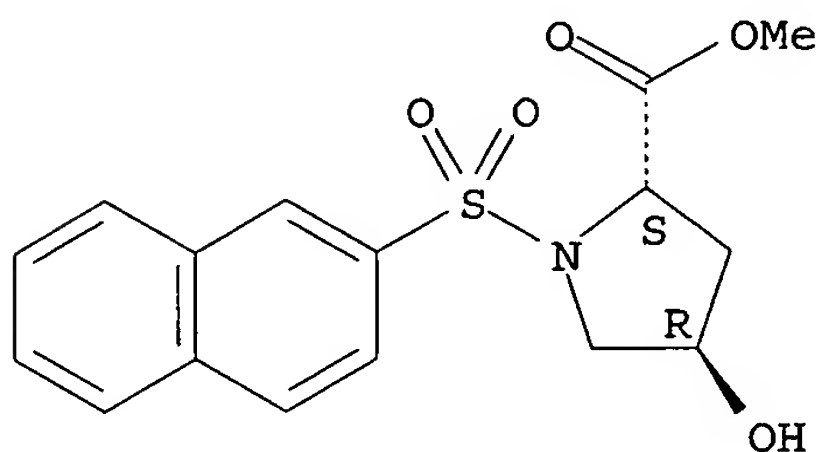
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrrolidinethiols and analogs as metalloprotease inhibitors)

RN 391671-83-3 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)-  
(9CI) (CA INDEX NAME)

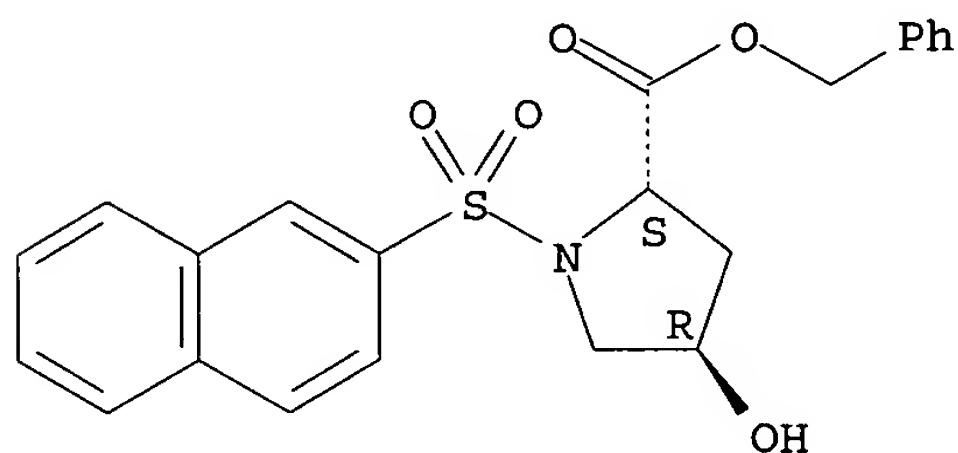
Absolute stereochemistry.



RN 391671-85-5 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester,  
(4R)- (9CI) (CA INDEX NAME)

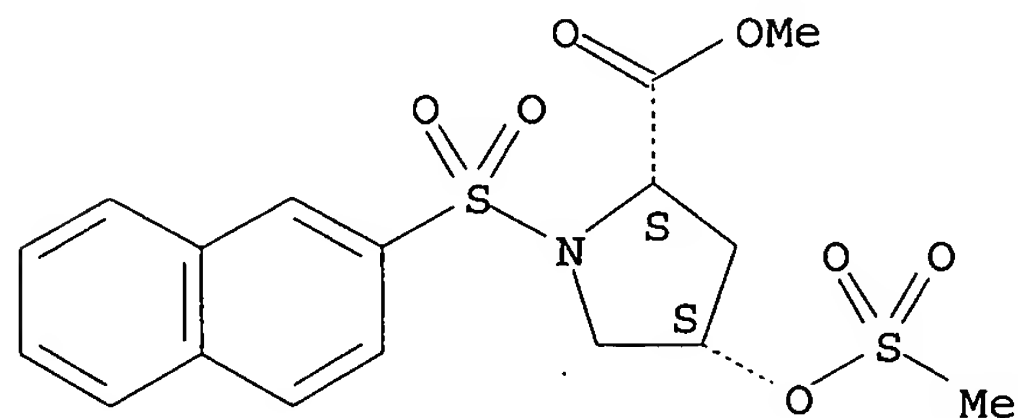
Absolute stereochemistry.



RN 391671-90-2 HCAPLUS

CN L-Proline, 4-[(methylsulfonyl)oxy]-1-(2-naphthalenylsulfonyl)-, methyl  
ester, (4S)- (9CI) (CA INDEX NAME)

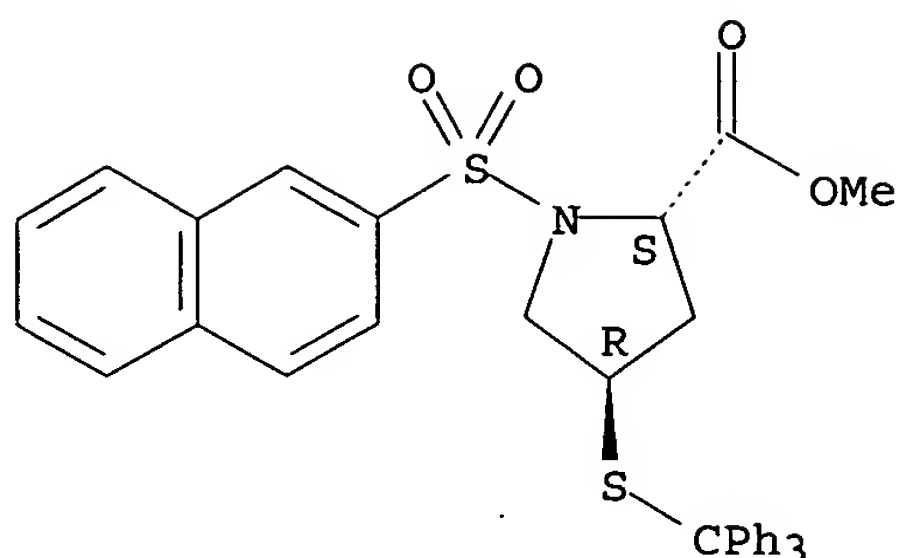
Absolute stereochemistry.



RN 391671-92-4 HCAPLUS

CN L-Proline, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl  
ester, (4R)- (9CI) (CA INDEX NAME)

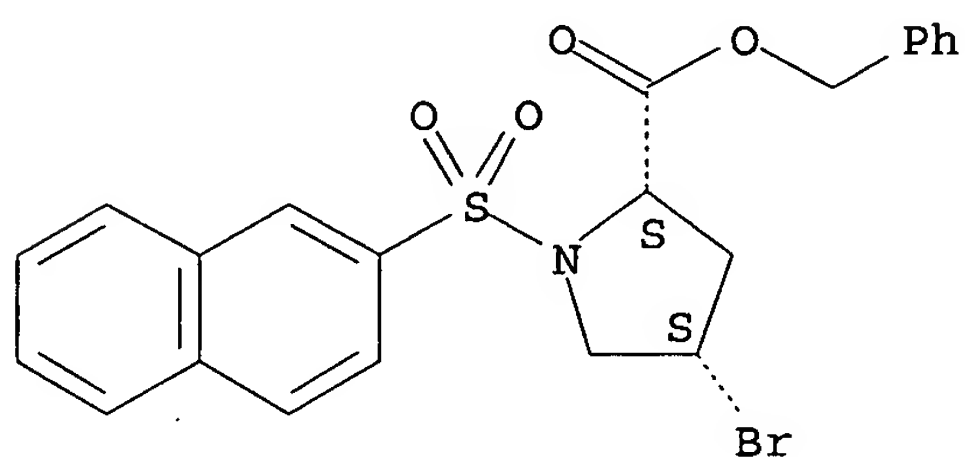
Absolute stereochemistry.



RN 391672-17-6 HCAPLUS

CN L-Proline, 4-bromo-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4S)-(9CI) (CA INDEX NAME)

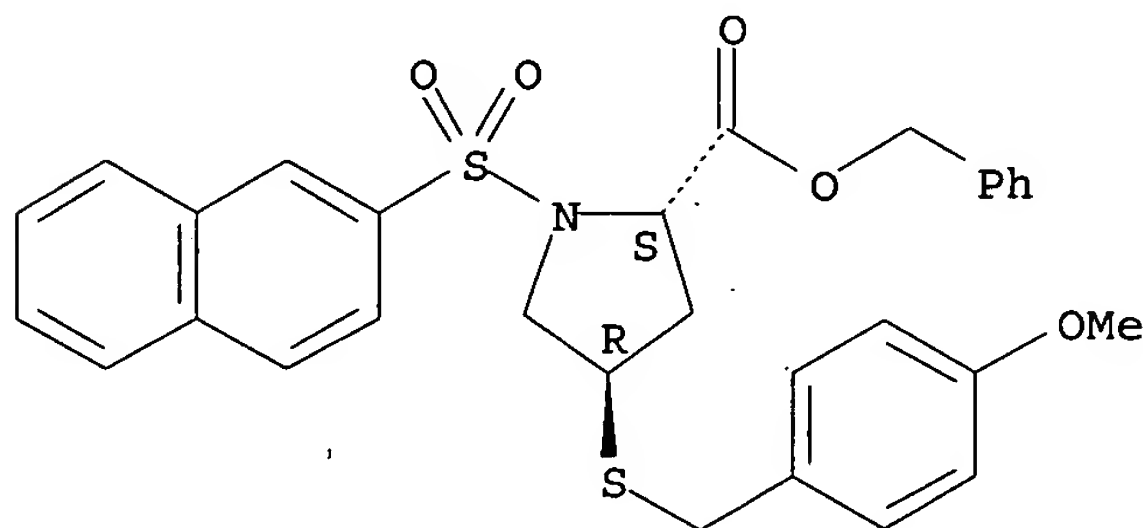
Absolute stereochemistry.



RN 391672-19-8 HCAPLUS

CN L-Proline, 4-[[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)-(9CI) (CA INDEX NAME)

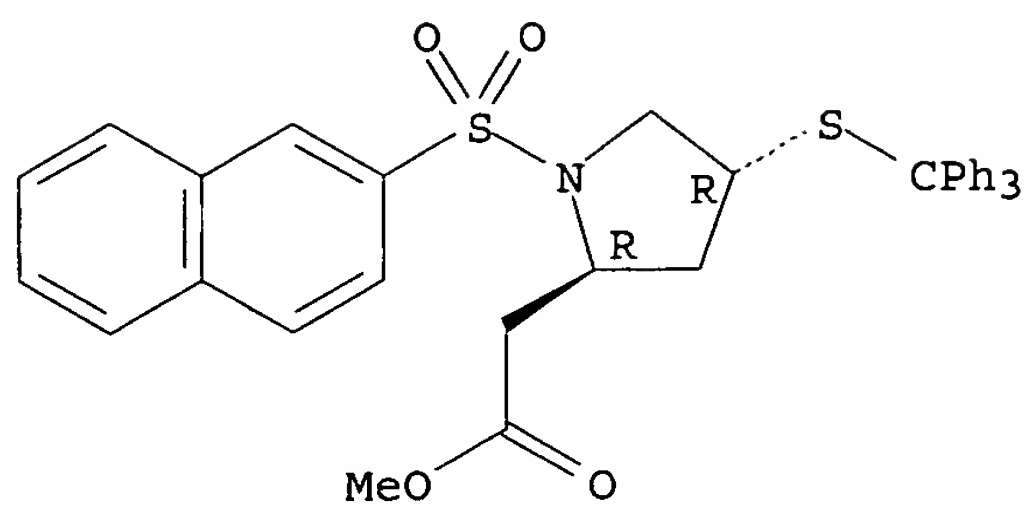
Absolute stereochemistry.



RN 393153-99-6 HCAPLUS

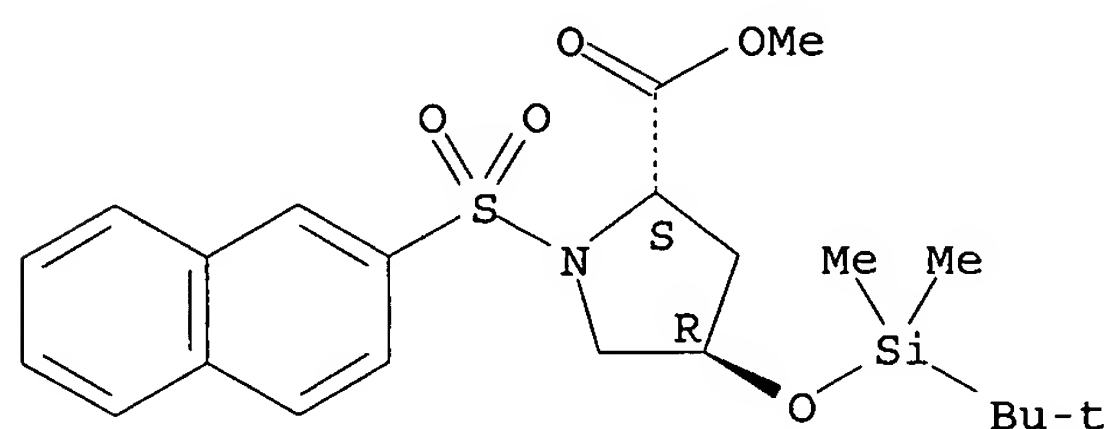
CN 2-Pyrrolidineacetic acid, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl ester, (2R,4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



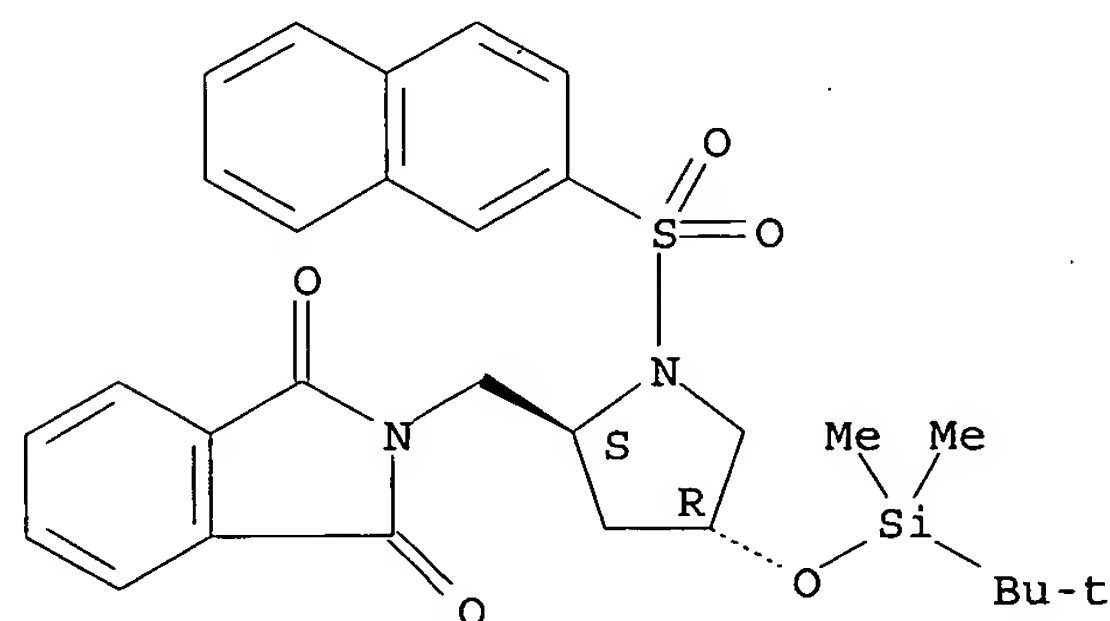
RN 393792-17-1 HCAPLUS  
 CN L-Proline, 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



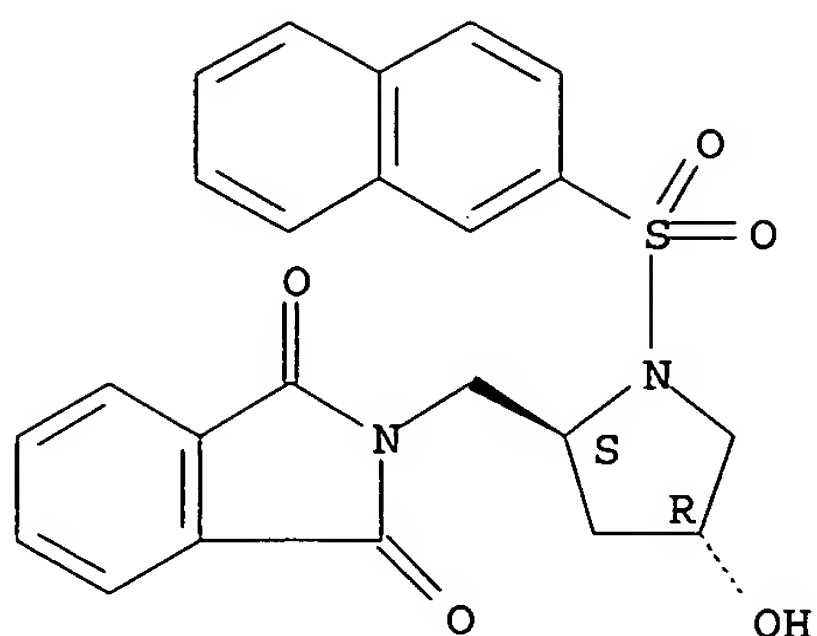
RN 393792-19-3 HCAPLUS  
 CN Pyrrolidine, 2-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-(2-naphthalenylsulfonyl)-, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



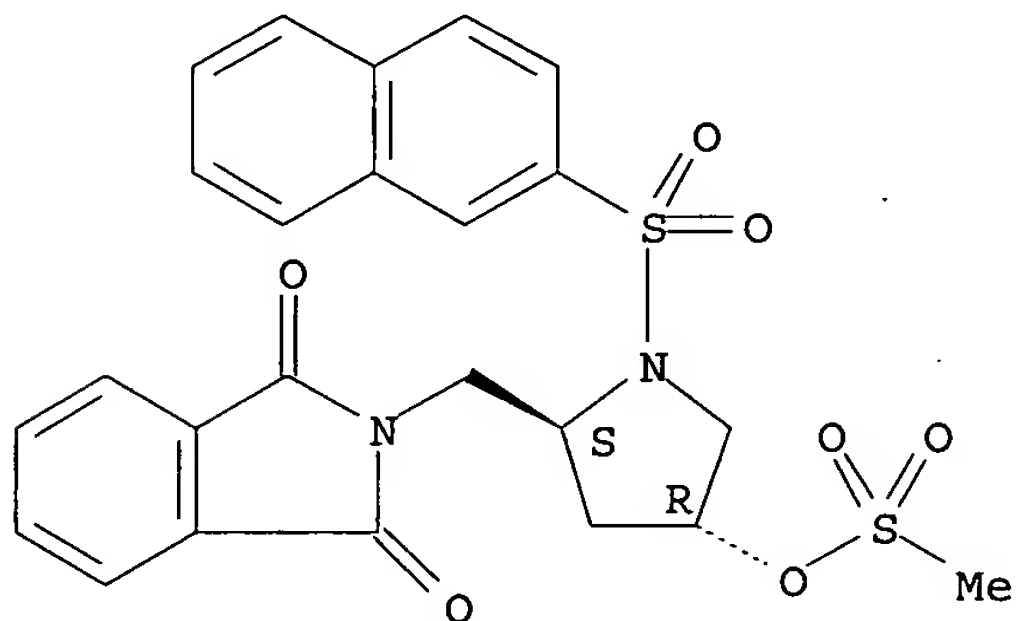
RN 393792-20-6 HCAPLUS  
 CN 3-Pyrrolidinol, 5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



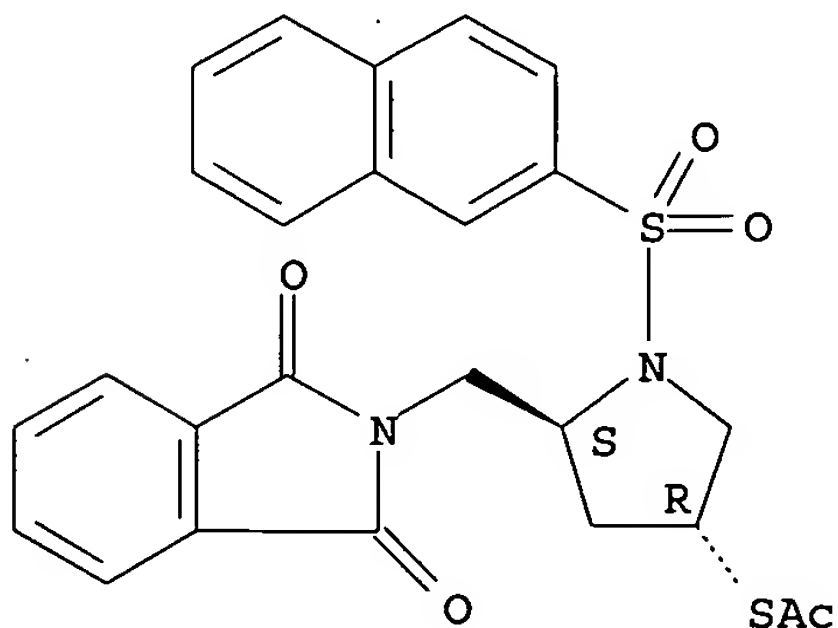
RN 393792-21-7 HCAPLUS  
 CN 3-Pyrrolidinol, 5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-1-(2-naphthalenylsulfonyl)-, methanesulfonate (ester), (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393792-22-8 HCAPLUS  
 CN Ethanethioic acid, S-[(3R,5S)-5-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-1-(2-naphthalenylsulfonyl)-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

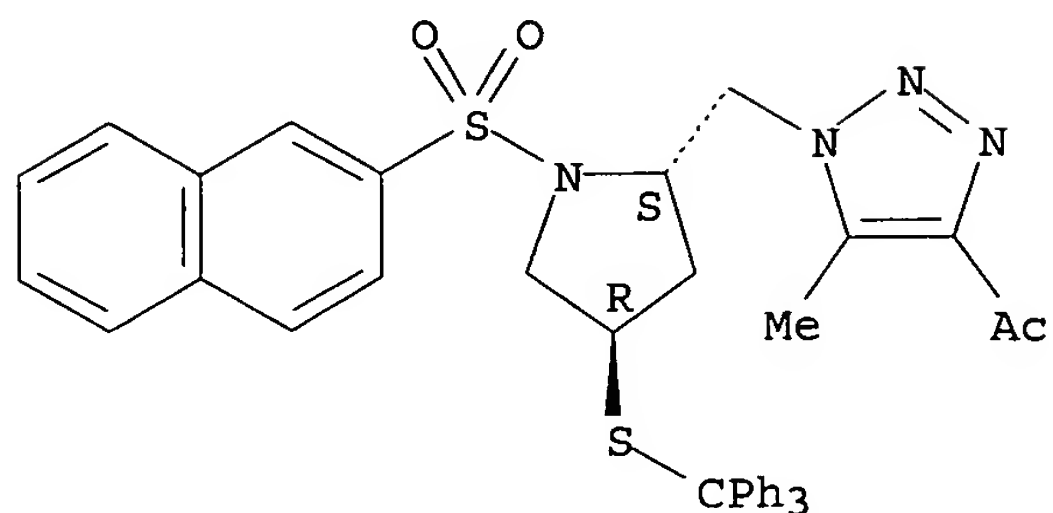
Absolute stereochemistry.



RN 393792-26-2 HCAPLUS  
 CN Pyrrolidine, 2-[(4-acetyl-5-methyl-1H-1,2,3-triazol-1-yl)methyl]-1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, (2S,4R)- (9CI) (CA INDEX NAME)

INDEX NAME)

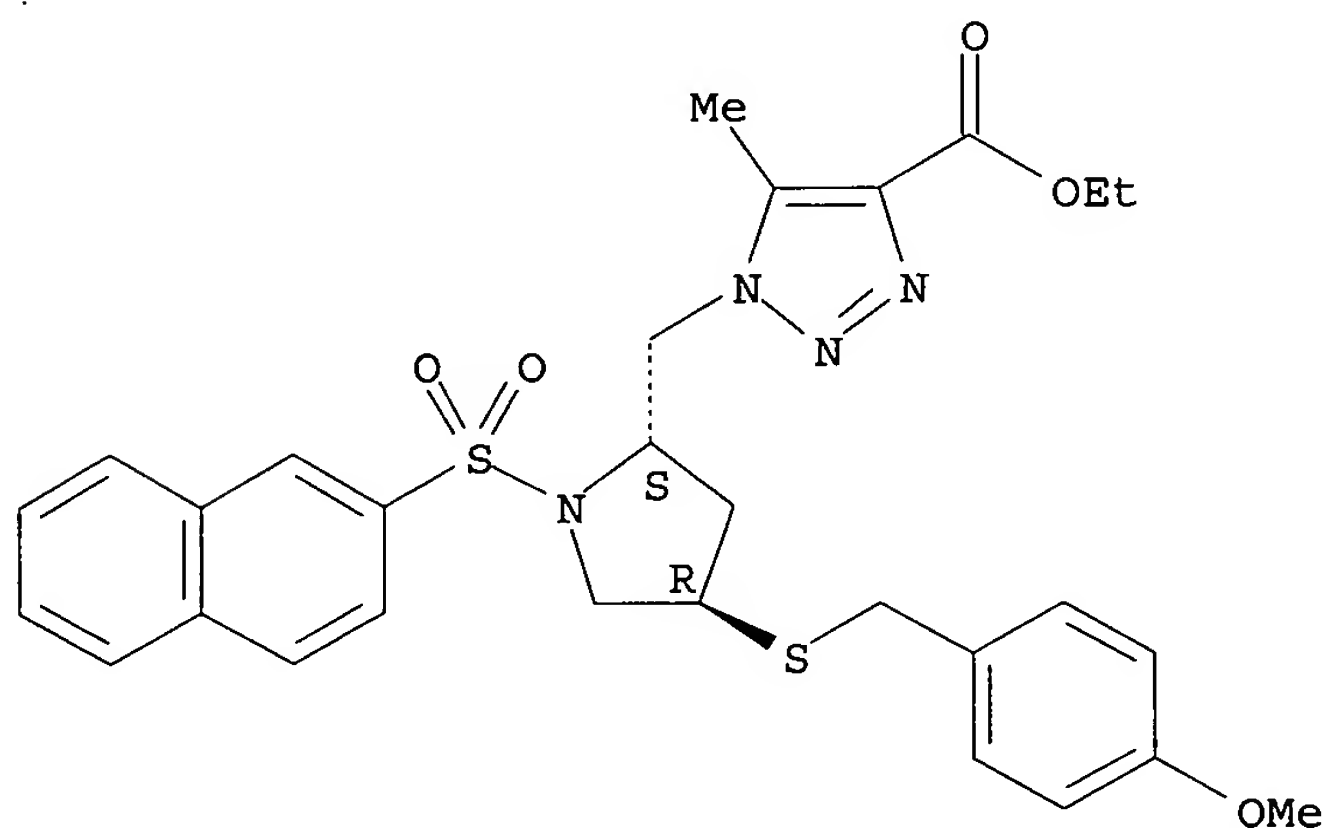
Absolute stereochemistry.



RN 393792-27-3 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxylic acid, 1-[[[(2S,4R)-4-[[[4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]-5-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

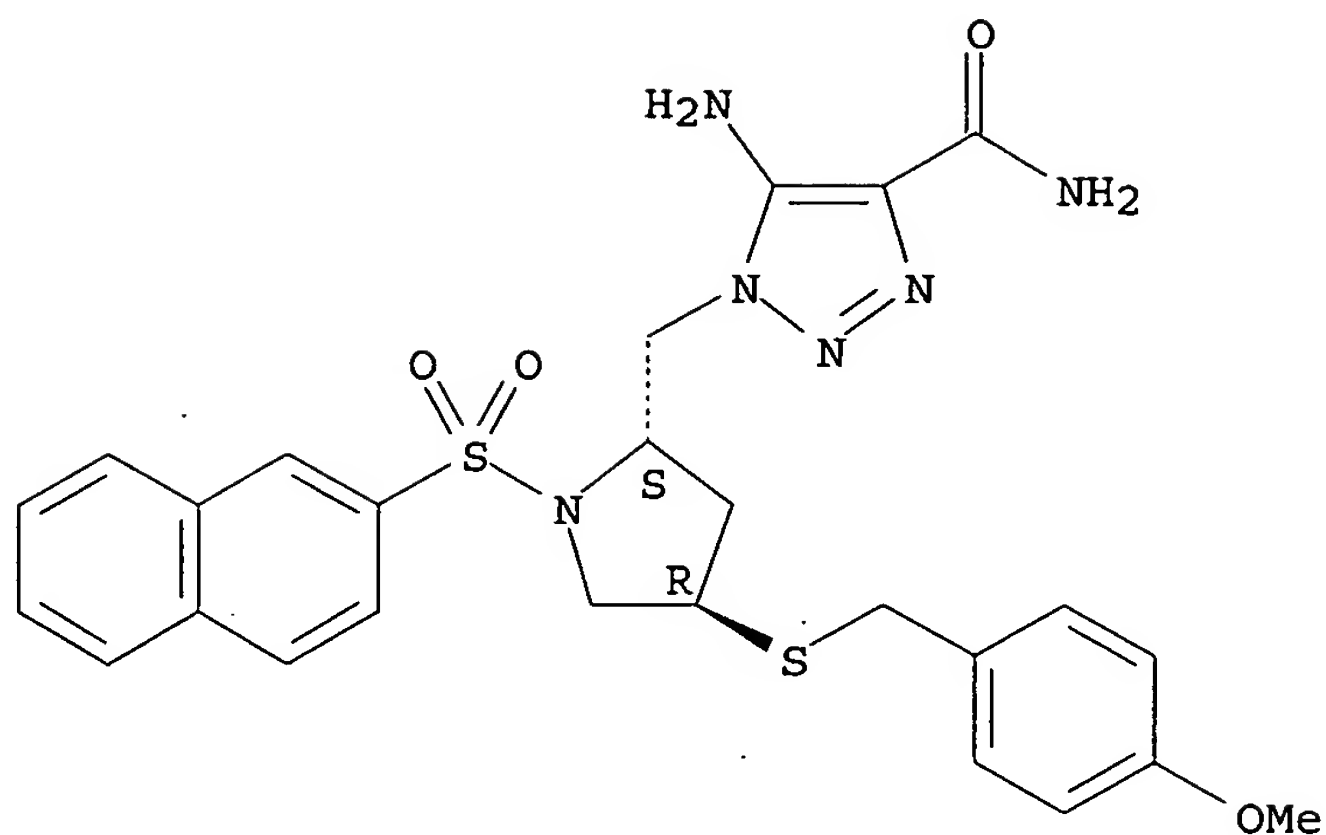


RN 393792-28-4 HCAPLUS

CN 1H-1,2,3-Triazole-4-carboxamide, 5-amino-1-[[[(2S,4R)-4-[[[4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

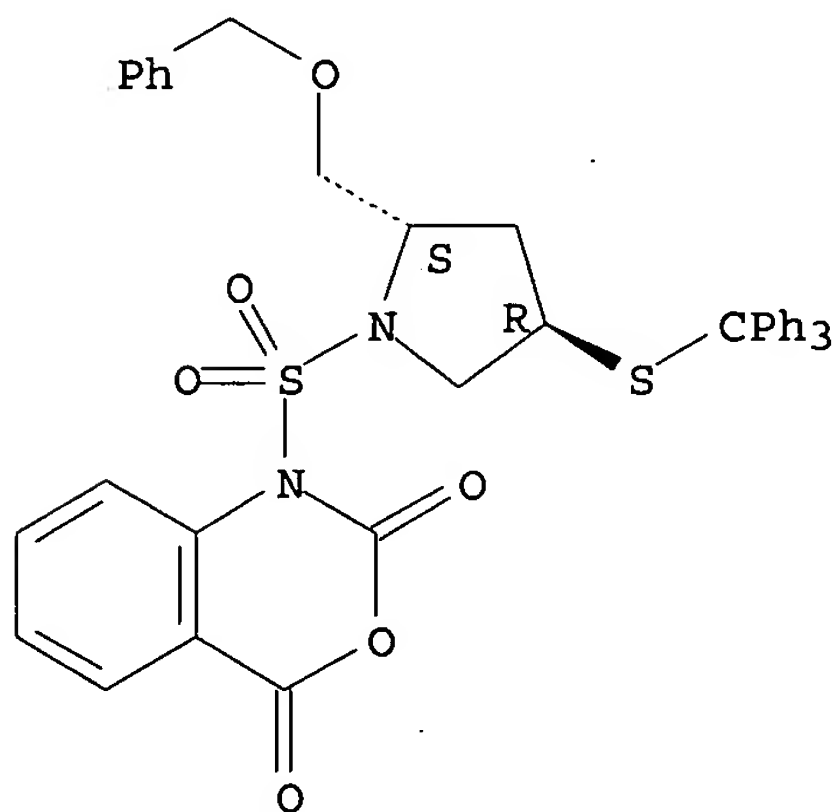




RN 393792-63-7 HCAPLUS

CN 2H-3,1-Benzoxazine-2,4(1H)-dione, 1-[[[(2S,4R)-2-[(phenylmethoxy)methyl]-4-[(triphenylmethyl)thio]-1-pyrrolidinyl]sulfonyl]- (9CI) (CA INDEX NAME)

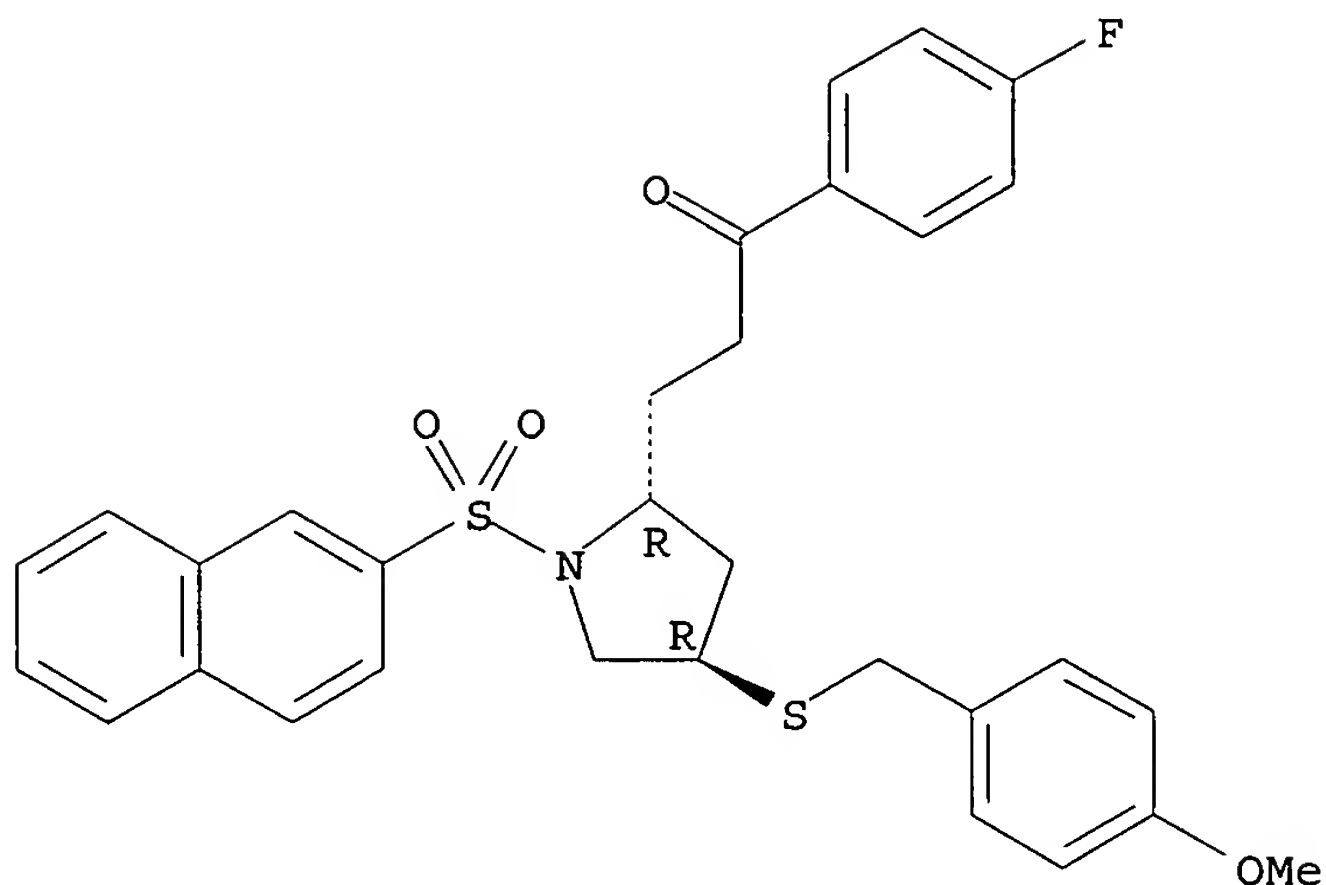
Absolute stereochemistry.



RN 393793-01-6 HCAPLUS

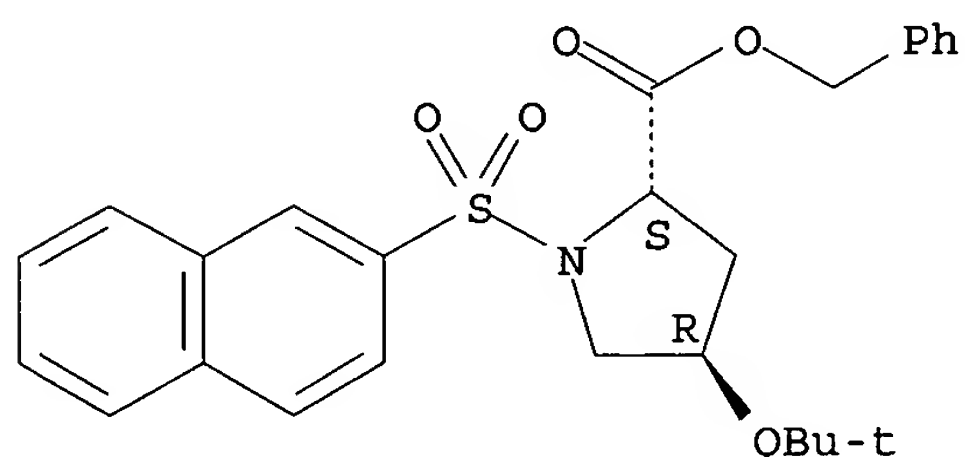
CN Pyrrolidine, 2-[3-(4-fluorophenyl)-3-oxopropyl]-4-[[[4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



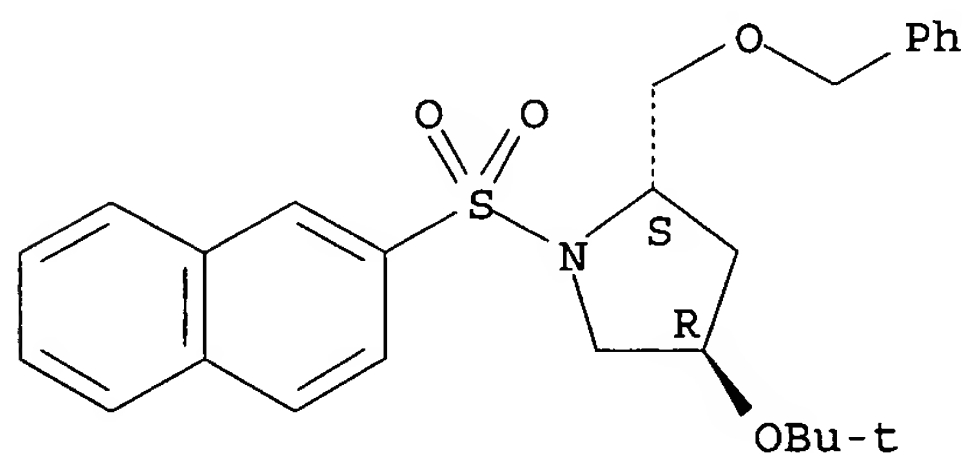
RN 393793-02-7 HCAPLUS  
 CN L-Proline, 4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



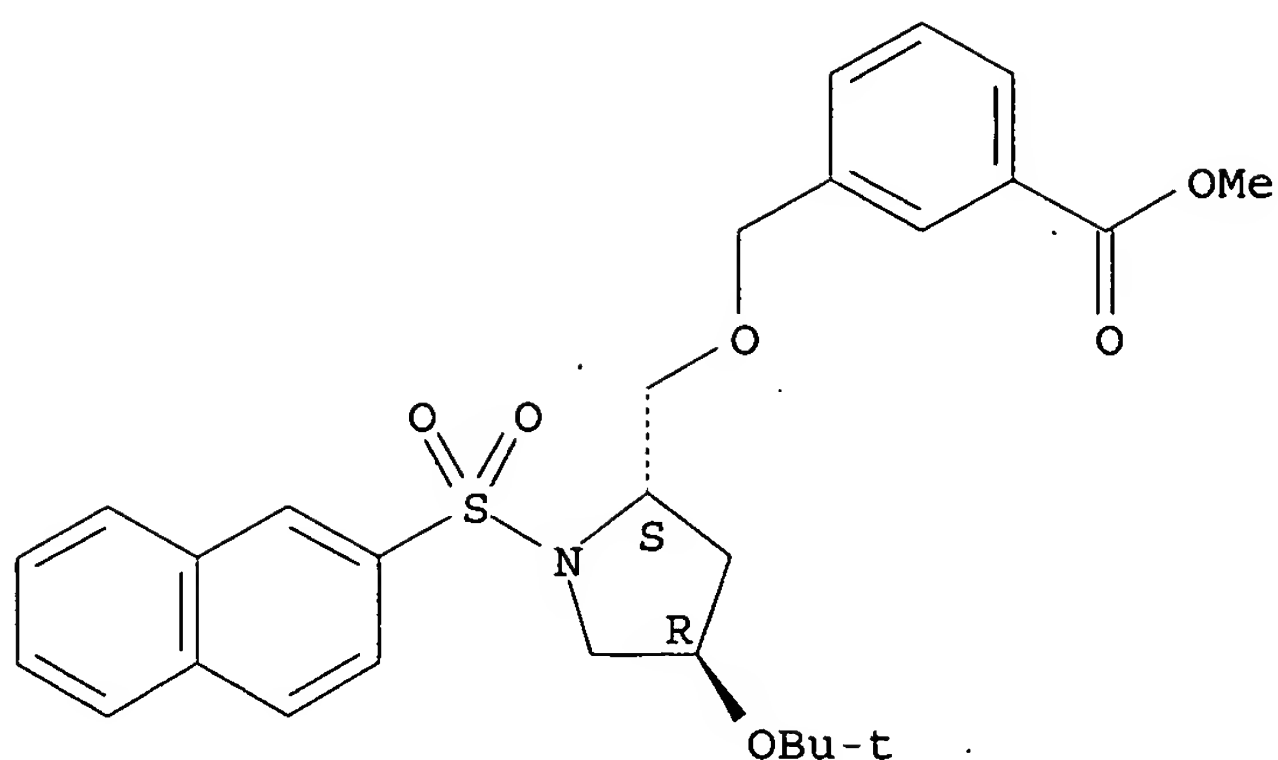
RN 393793-06-1 HCAPLUS  
 CN Pyrrolidine, 4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-2-[(phenylmethoxy)methyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393793-07-2 HCAPLUS  
 CN Benzoic acid, 3-[[[(2S,4R)-4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

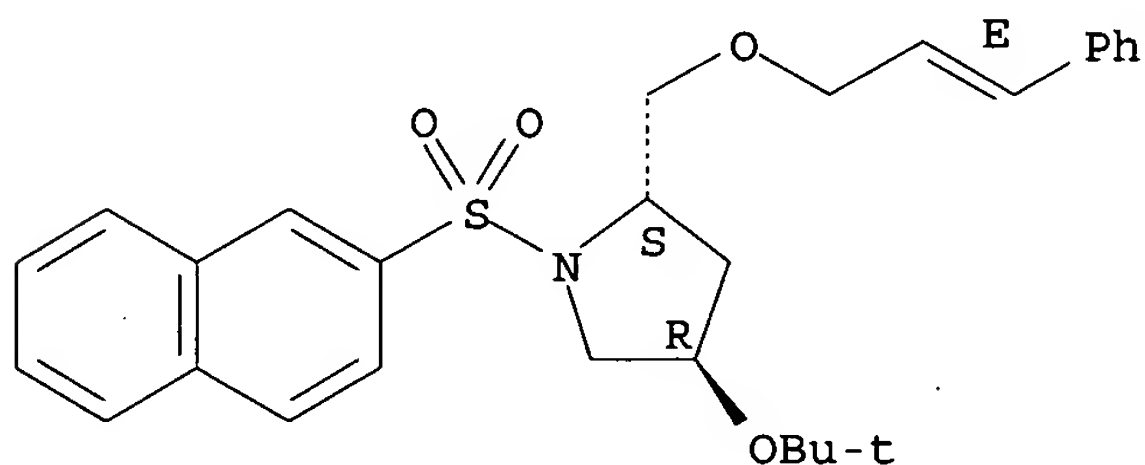
Absolute stereochemistry.



RN 393793-08-3 HCAPLUS

CN Pyrrolidine, 4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-2-[[[(2E)-3-phenyl-2-propenyl]oxy]methyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

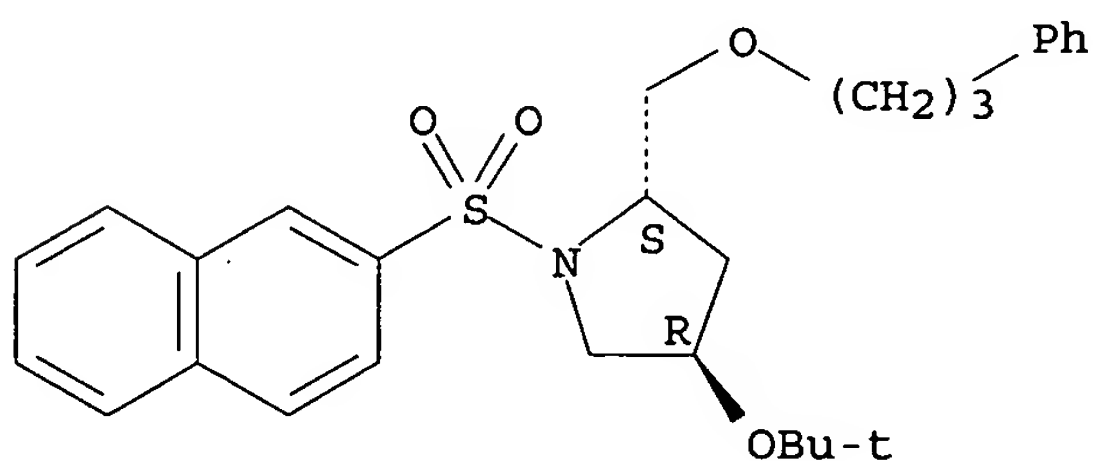
Absolute stereochemistry.  
Double bond geometry as shown.



RN 393793-09-4 HCAPLUS

CN Pyrrolidine, 4-(1,1-dimethylethoxy)-1-(2-naphthalenylsulfonyl)-2-[(3-phenylpropoxy)methyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

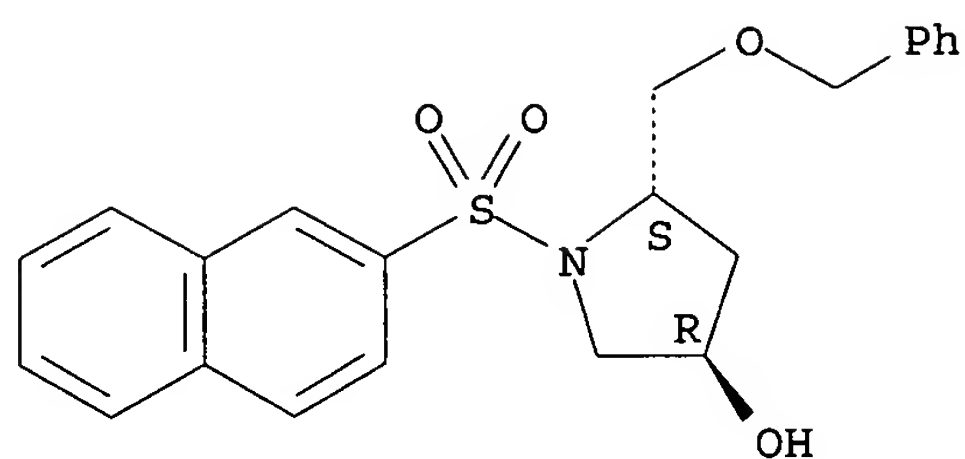
Absolute stereochemistry.



RN 393793-13-0 HCAPLUS

CN 3-Pyrrolidinol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

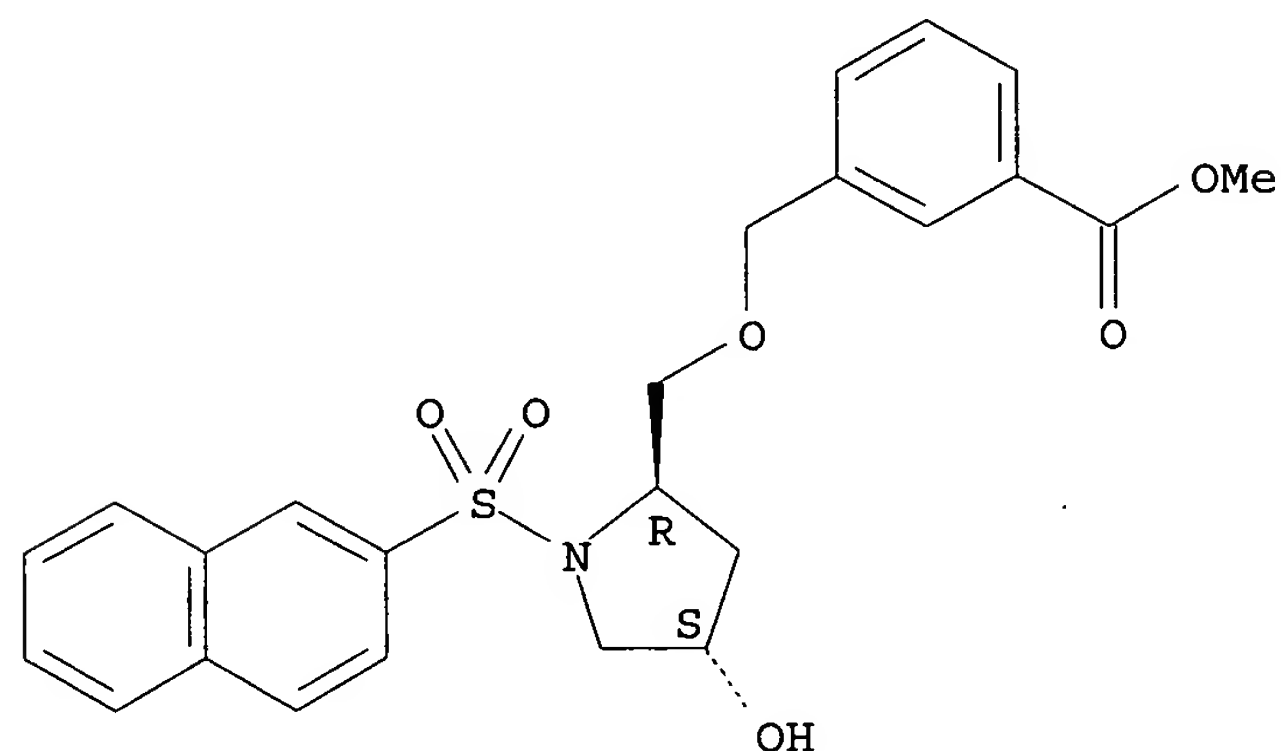
Absolute stereochemistry.



RN 393793-14-1 HCAPLUS

CN Benzoic acid, 3-[[[(2R,4S)-4-hydroxy-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

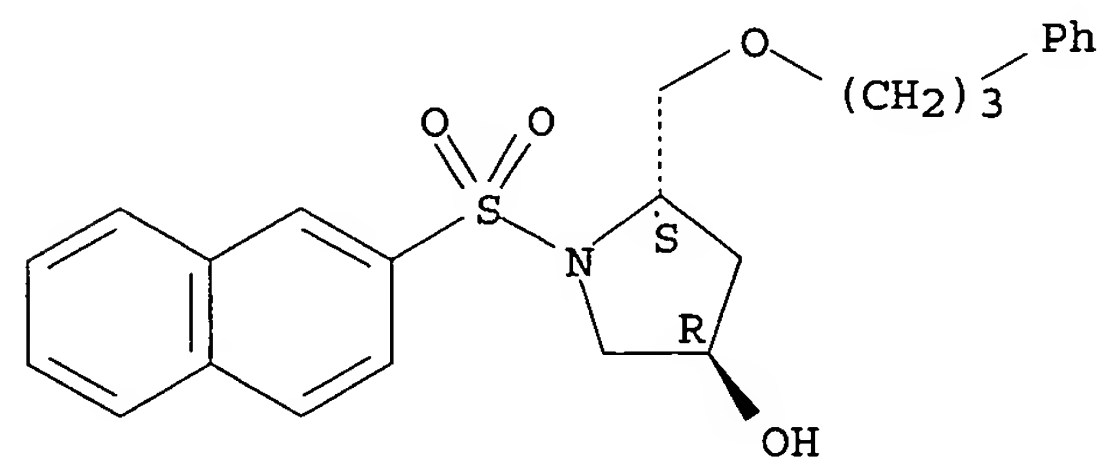
Absolute stereochemistry.



RN 393793-15-2 HCAPLUS

CN 3-Pyrrolidinol, 1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-, (3R,5S)- (9CI) (CA INDEX NAME)

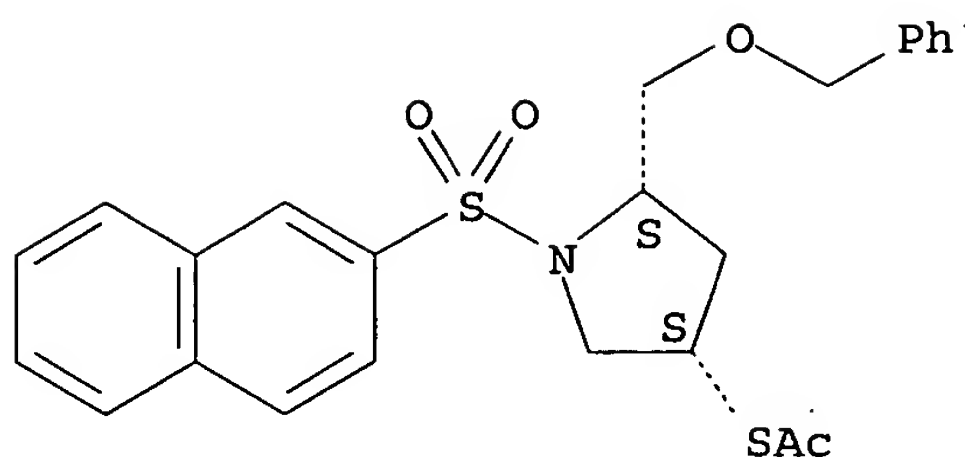
Absolute stereochemistry.



RN 393793-18-5 HCAPLUS

CN Ethanethioic acid, S-[(3S,5S)-1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

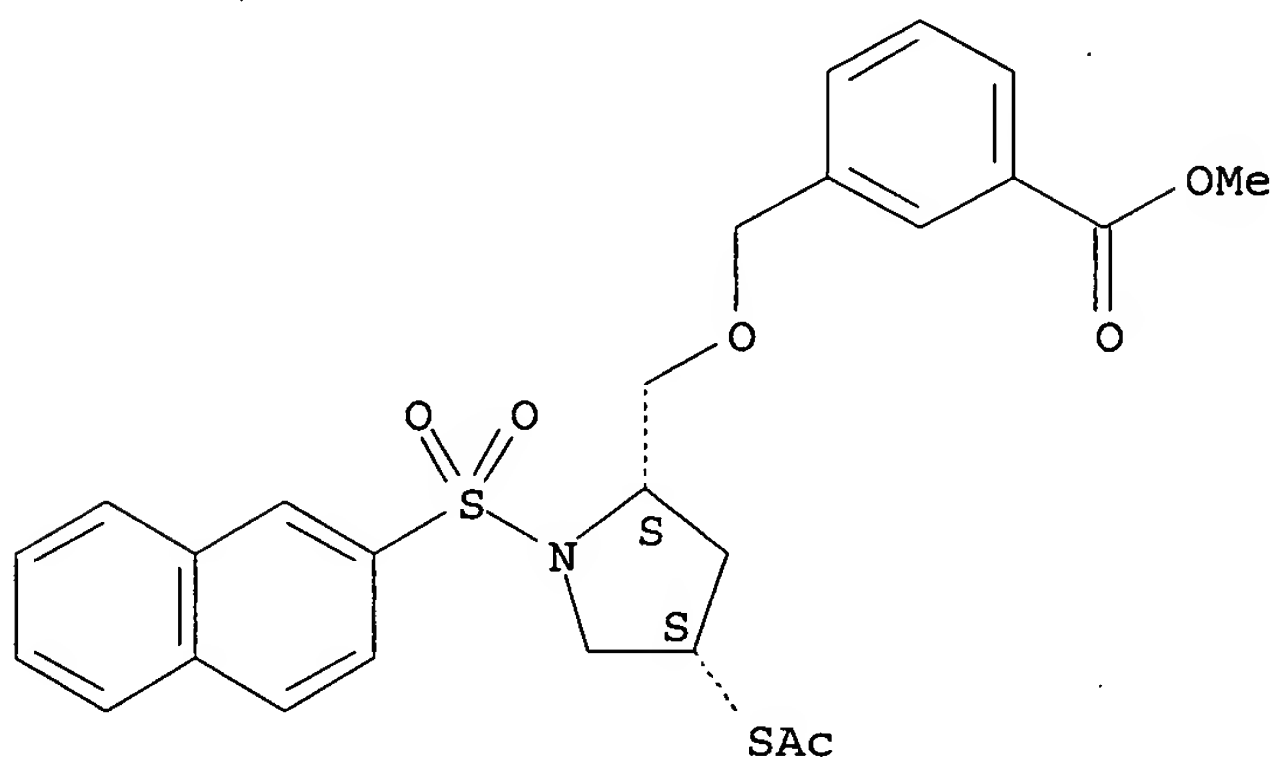
Absolute stereochemistry.



RN 393793-19-6 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4S)-4-(acetylthio)-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

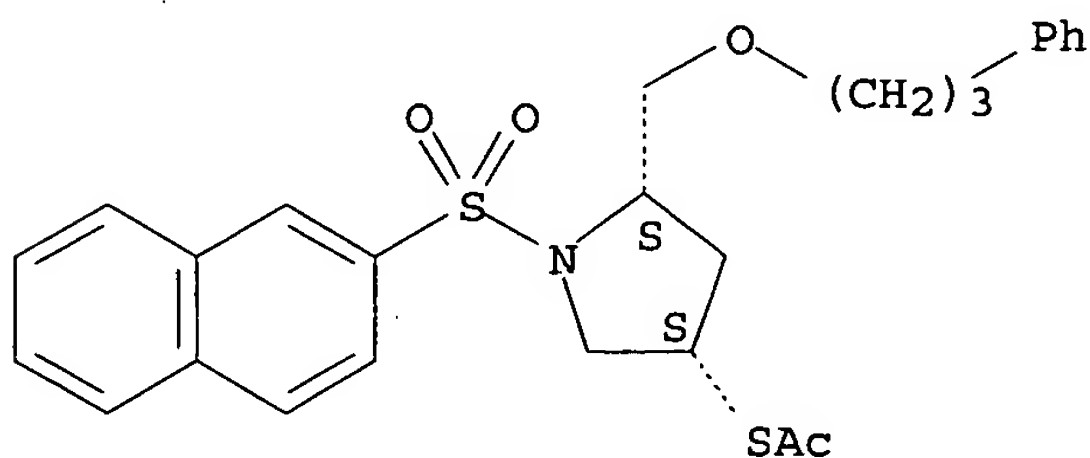
Absolute stereochemistry.



RN 393793-20-9 HCAPLUS

CN Ethanethioic acid, S-[(3S,5S)-1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

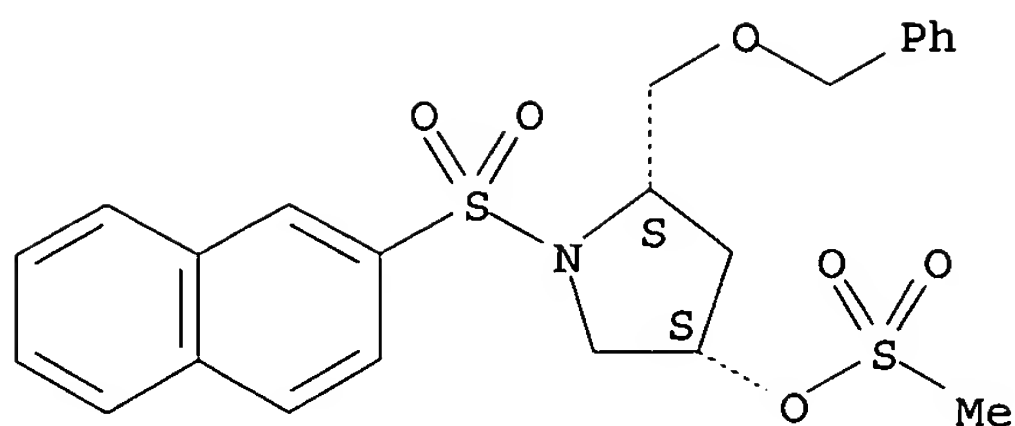
Absolute stereochemistry.



RN 393793-23-2 HCAPLUS

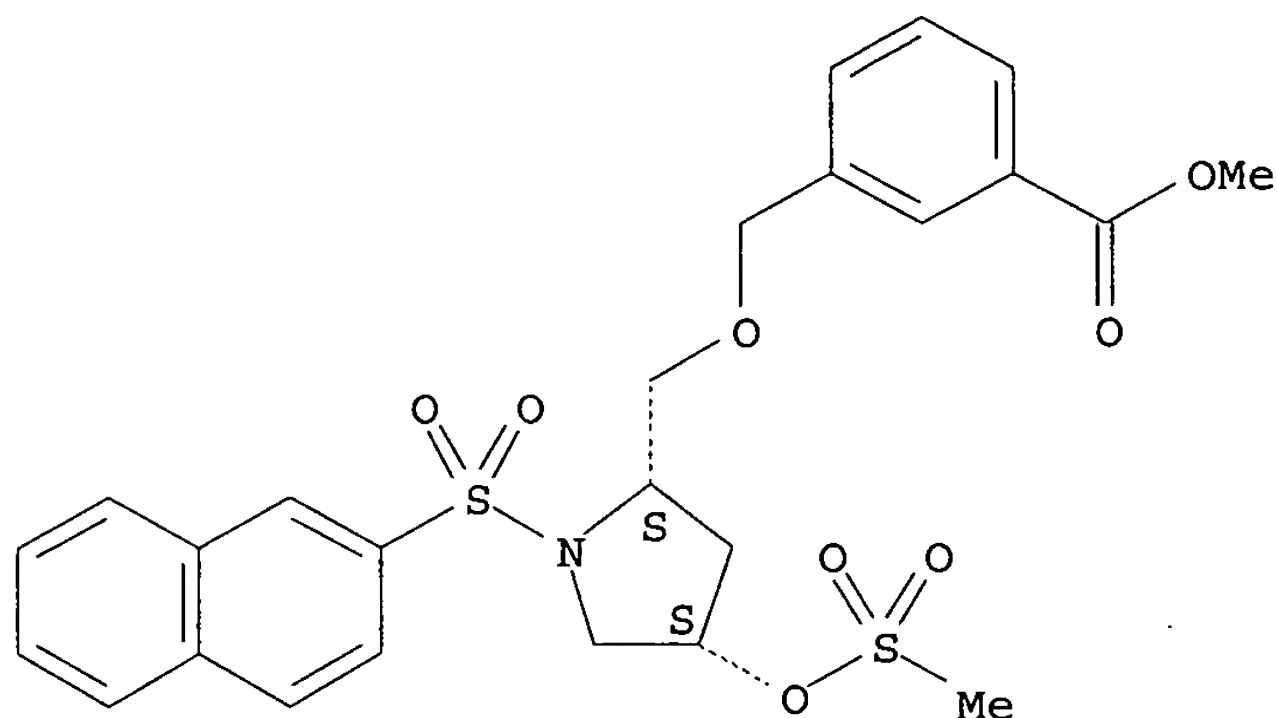
CN 3-Pyrrolidinol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, methanesulfonate (ester), (3S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



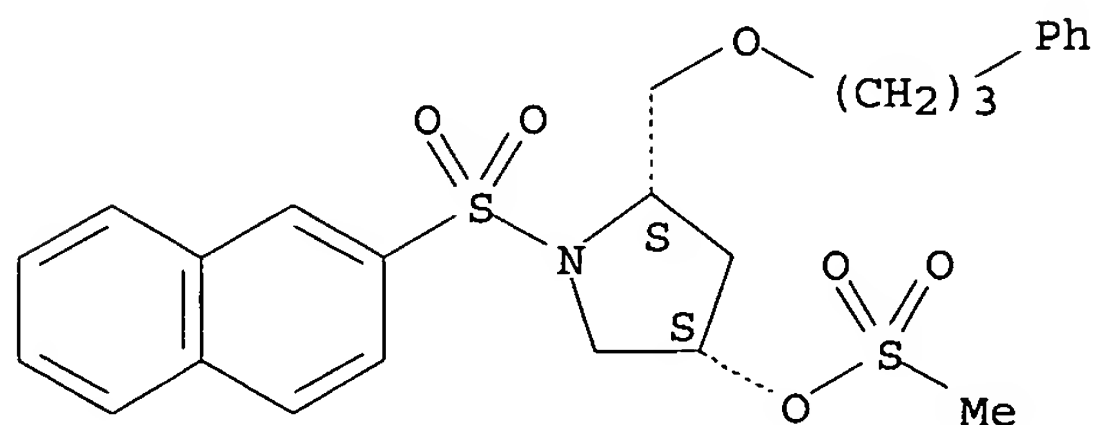
RN 393793-24-3 HCAPLUS  
 CN Benzoic acid, 3-[[[(2S,4S)-4-[(methanesulfonyl)oxy]-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



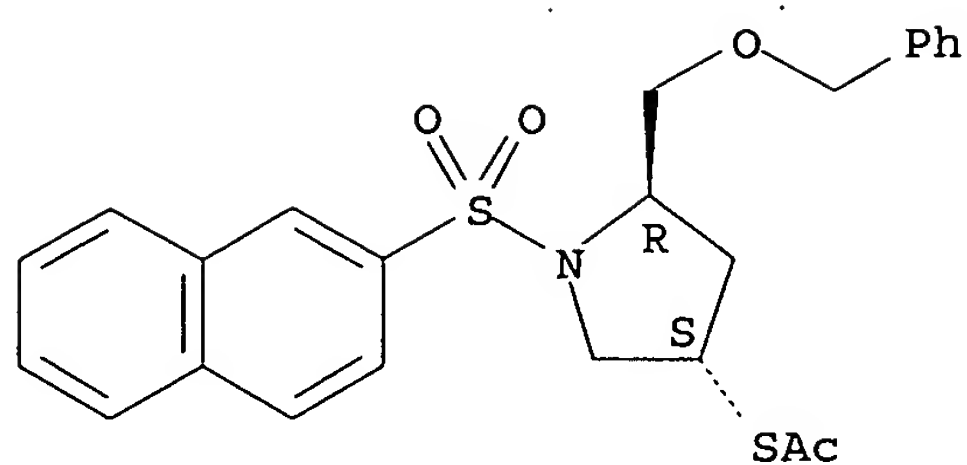
RN 393793-25-4 HCAPLUS  
 CN 3-Pyrrolidinol, 1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-, methanesulfonate (ester), (3S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393793-27-6 HCAPLUS  
 CN Ethanethioic acid, S-[(3S,5R)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

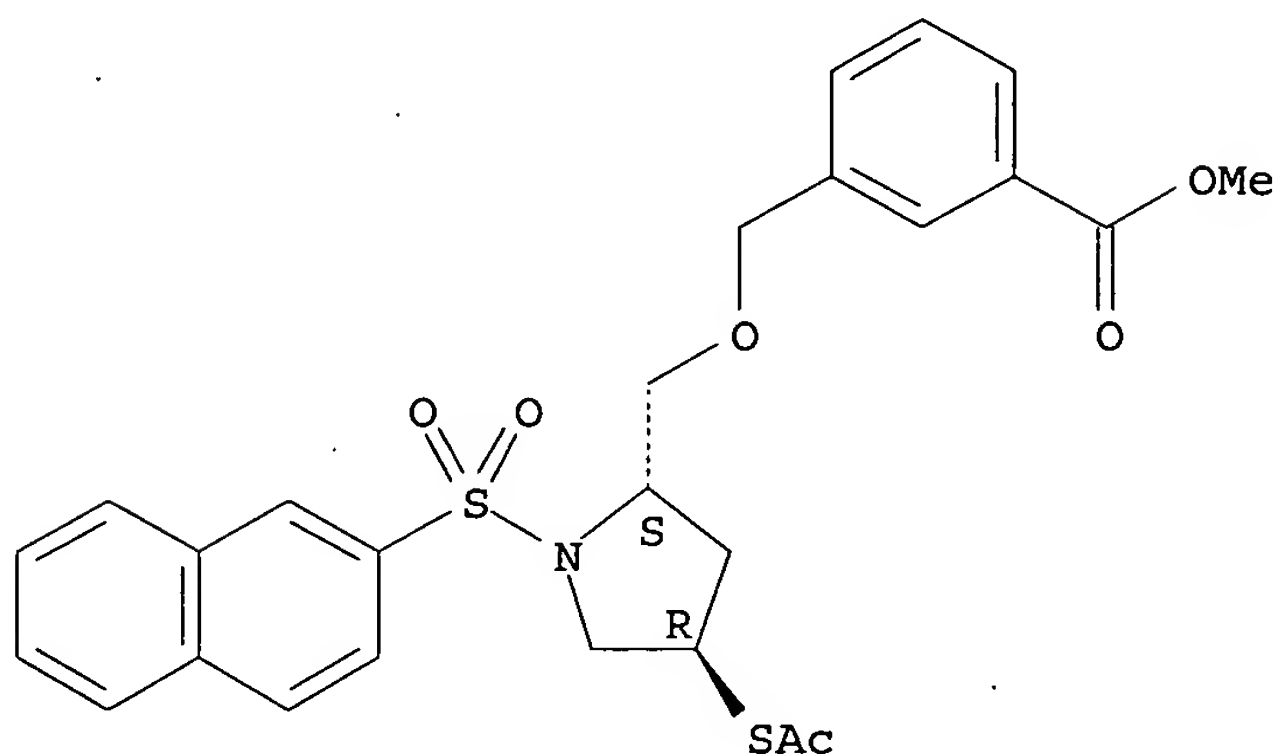
Absolute stereochemistry.



RN 393793-28-7 HCAPLUS

CN Benzoic acid, 3-[[[(2S,4R)-4-(acetylthio)-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]methoxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)

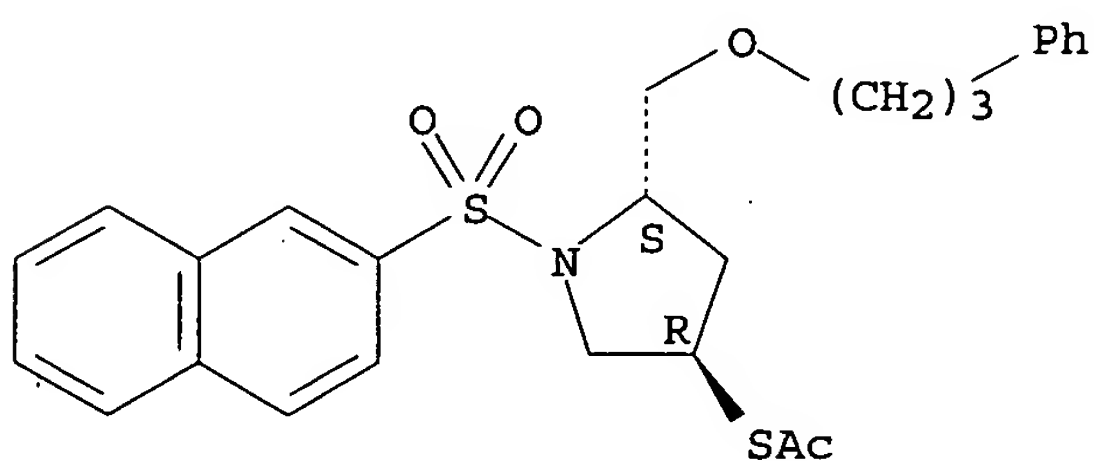
Absolute stereochemistry.



RN 393793-29-8 HCAPLUS

CN Ethanethioic acid, S-[(3R,5S)-1-(2-naphthalenylsulfonyl)-5-[(3-phenylpropoxy)methyl]-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

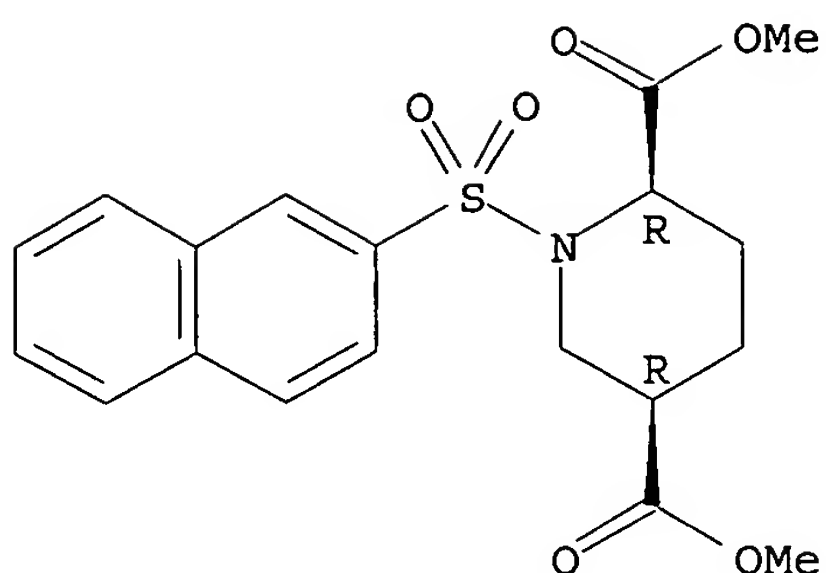
Absolute stereochemistry.



RN 393793-33-4 HCAPLUS

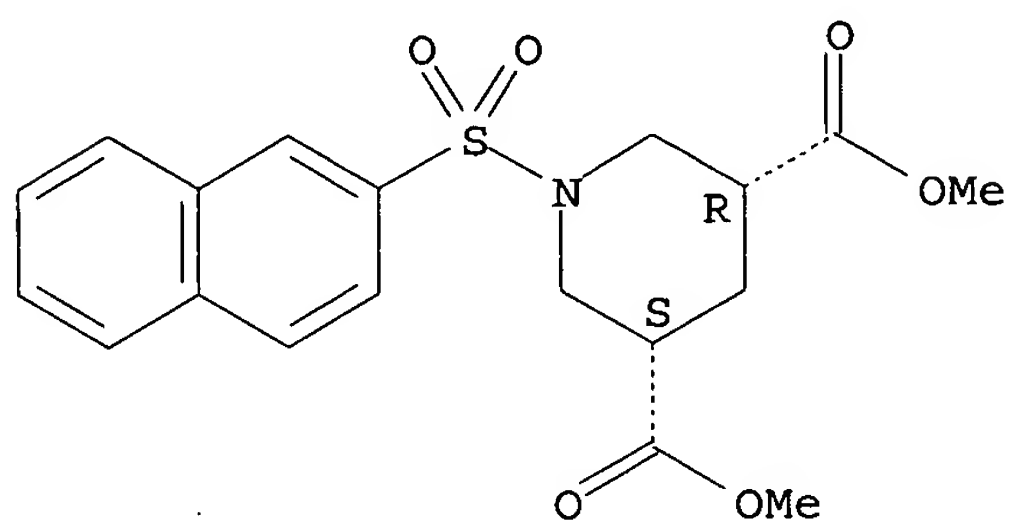
CN 2,5-Piperidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, dimethyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



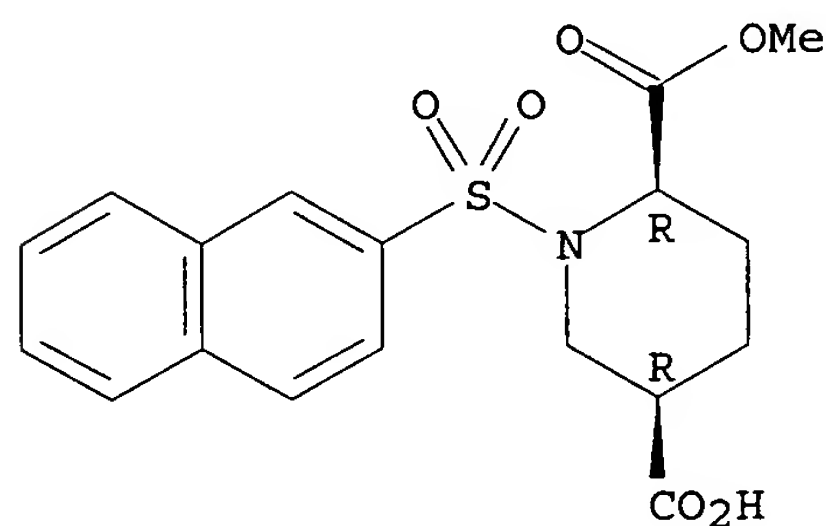
RN 393793-34-5 HCAPLUS  
 CN 3,5-Piperidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, dimethyl ester, (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 393793-36-7 HCAPLUS  
 CN 2,5-Piperidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, 2-methyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

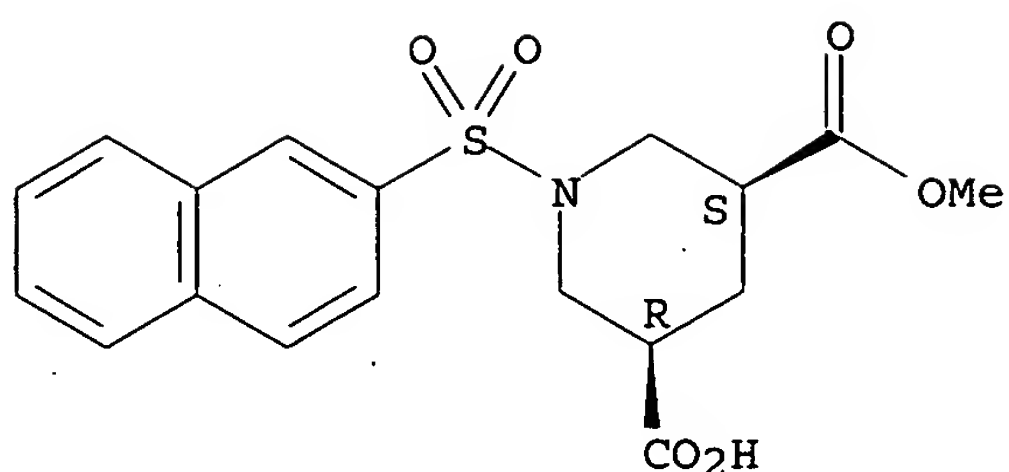
Relative stereochemistry.



RN 393793-37-8 HCAPLUS  
 CN 3,5-Piperidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, monomethyl ester, (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

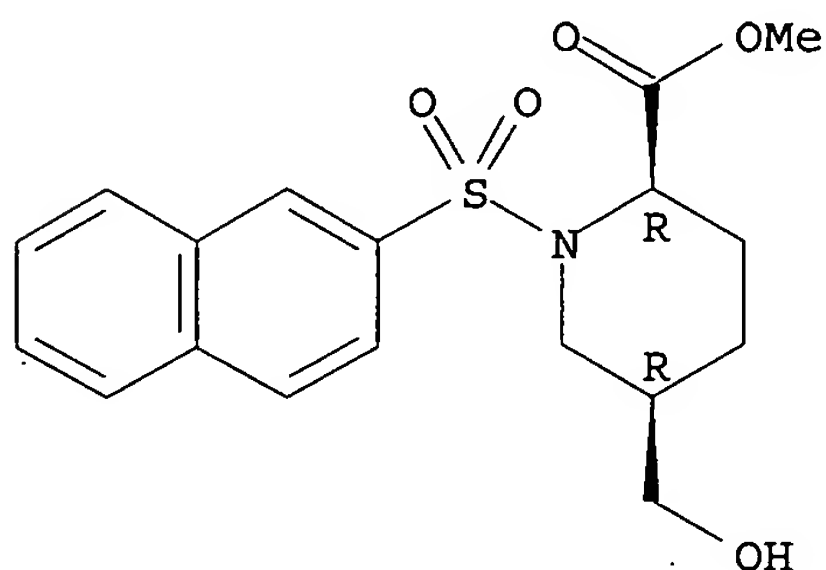




RN 393793-39-0 HCAPLUS

CN 2-Piperidinecarboxylic acid, 5-(hydroxymethyl)-1-(2-naphthalenylsulfonyl)-, methyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

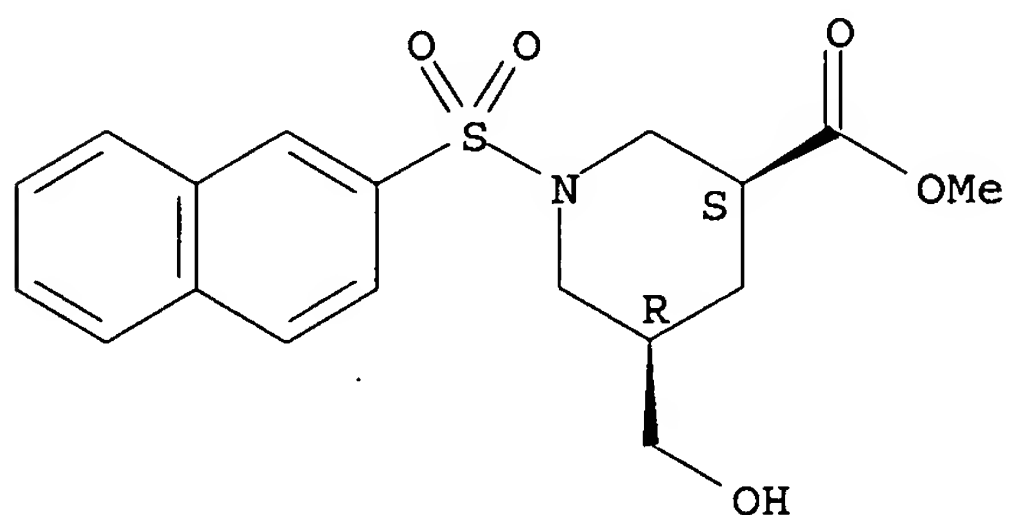
Relative stereochemistry.



RN 393793-40-3 HCAPLUS

CN 3-Piperidinecarboxylic acid, 5-(hydroxymethyl)-1-(2-naphthalenylsulfonyl)-, methyl ester, (3R,5S)-rel- (9CI) (CA INDEX NAME)

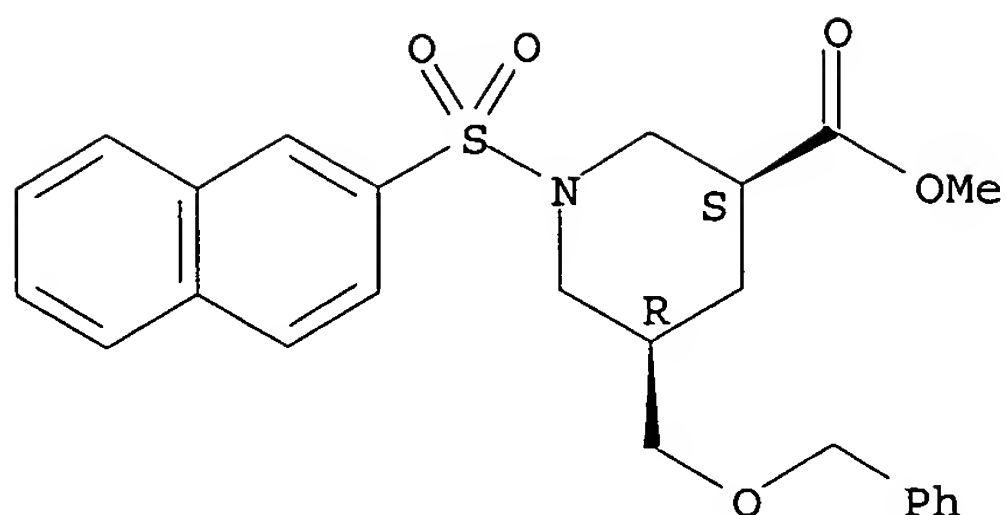
Relative stereochemistry.



RN 393793-41-4 HCAPLUS

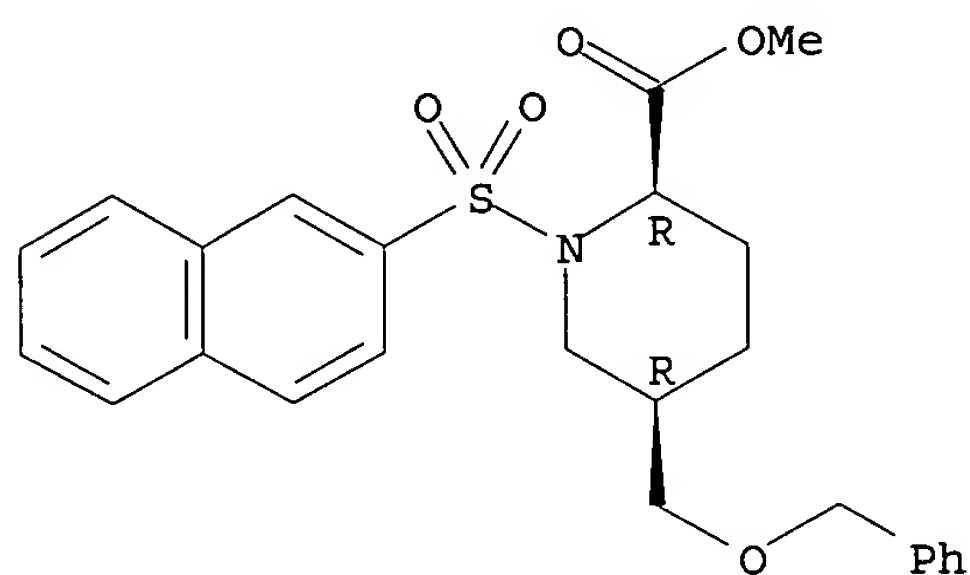
CN 3-Piperidinecarboxylic acid, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-, methyl ester, (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



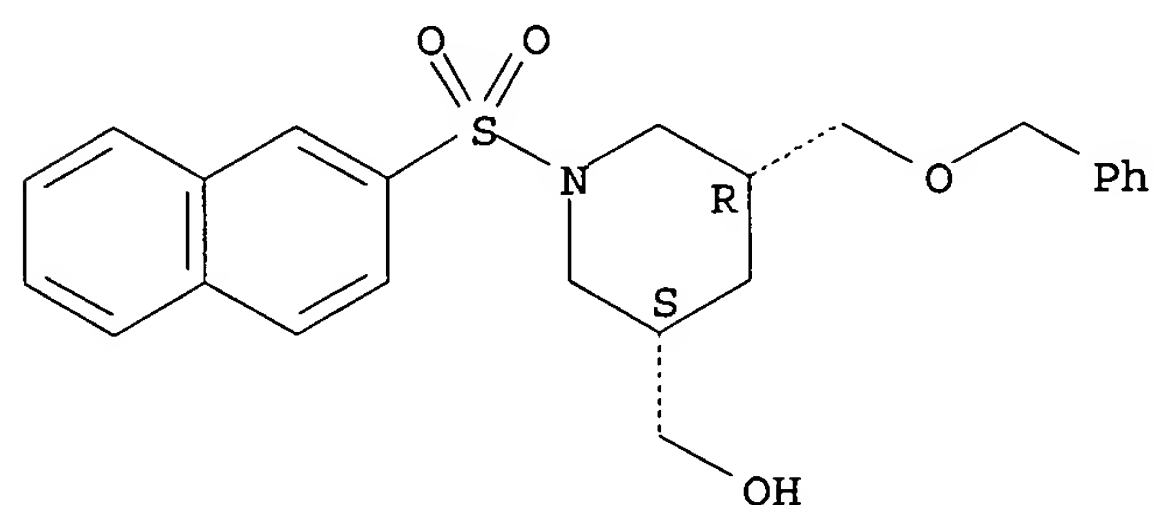
RN 393793-42-5 HCAPLUS  
 CN 2-Piperidinecarboxylic acid, 1-(2-naphthalenylsulfonyl)-5-  
 [(phenylmethoxy)methyl]-, methyl ester, (2R,5R)-rel- (9CI) (CA INDEX  
 NAME)

Relative stereochemistry.



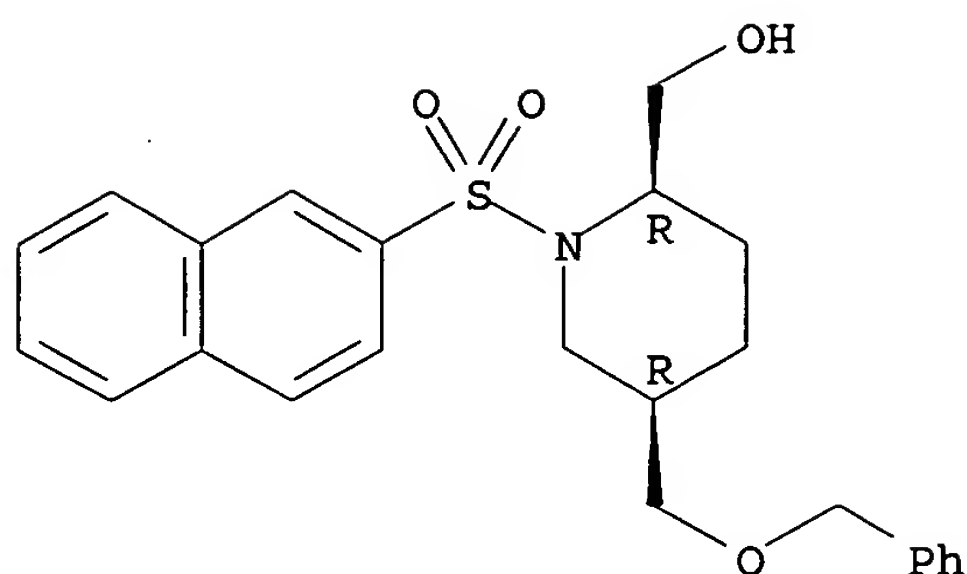
RN 393793-44-7 HCAPLUS  
 CN 3-Piperidinemethanol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-  
 , (3R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



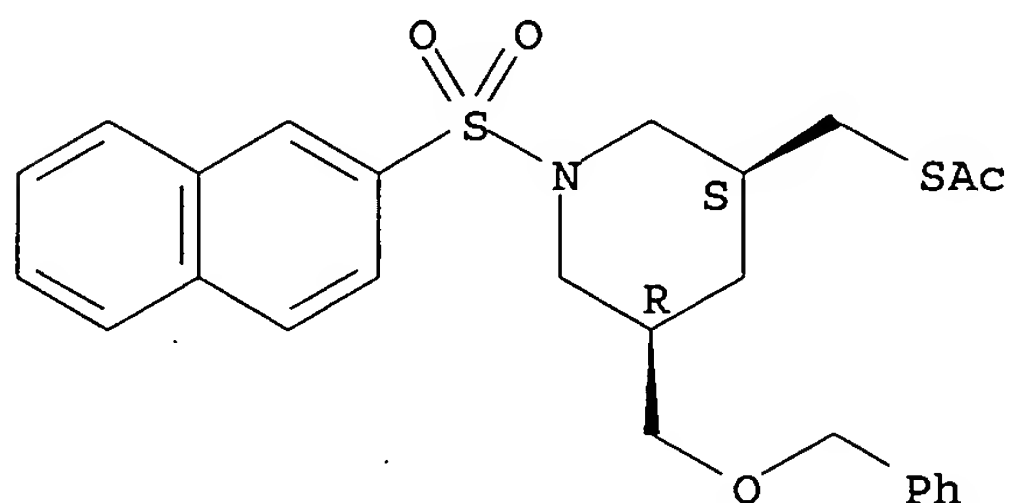
RN 393793-45-8 HCAPLUS  
 CN 2-Piperidinemethanol, 1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-  
 , (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



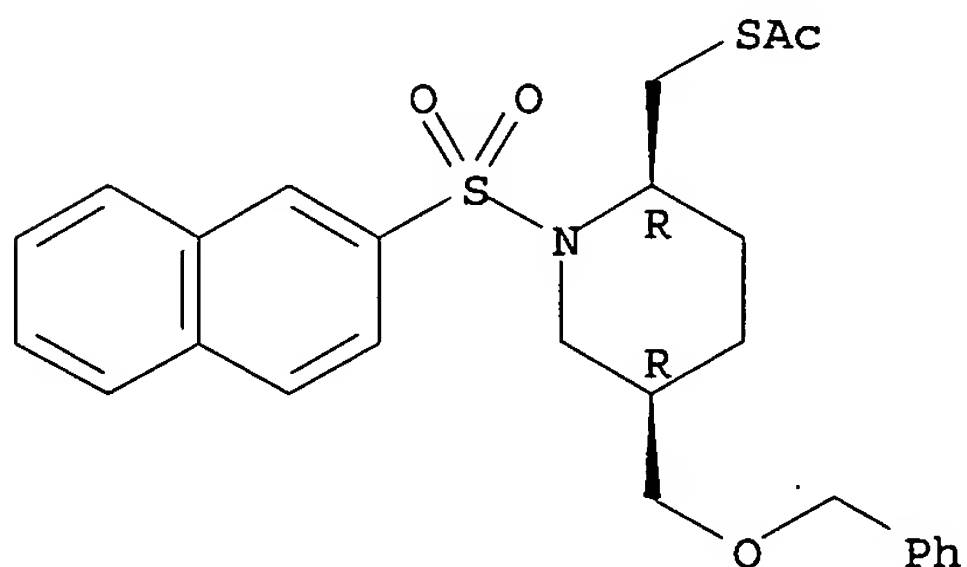
RN 393793-47-0 HCAPLUS  
 CN Ethanethioic acid, S-[[[(3R,5S)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-3-piperidinyll methyl] ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



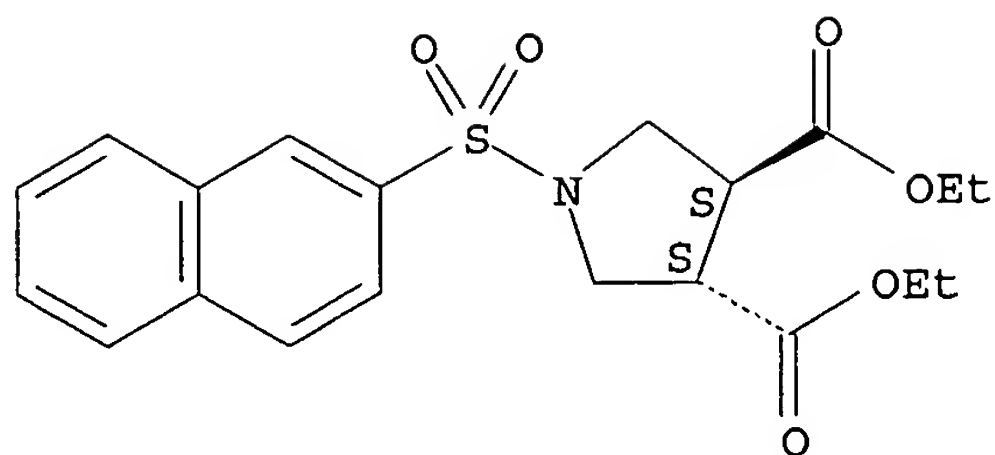
RN 393793-48-1 HCAPLUS  
 CN Ethanethioic acid, S-[[[(2R,5R)-1-(2-naphthalenylsulfonyl)-5-[(phenylmethoxy)methyl]-2-piperidinyll methyl] ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 393793-51-6 HCAPLUS  
 CN 3,4-Pyrrolidinedicarboxylic acid, 1-(2-naphthalenylsulfonyl)-, diethyl ester, (3R,4R)-rel- (9CI) (CA INDEX NAME)

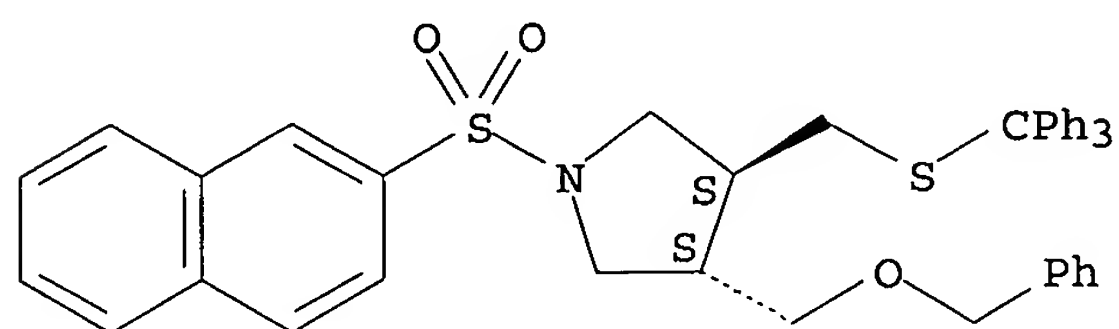
Relative stereochemistry.



RN 393793-60-7 HCAPLUS

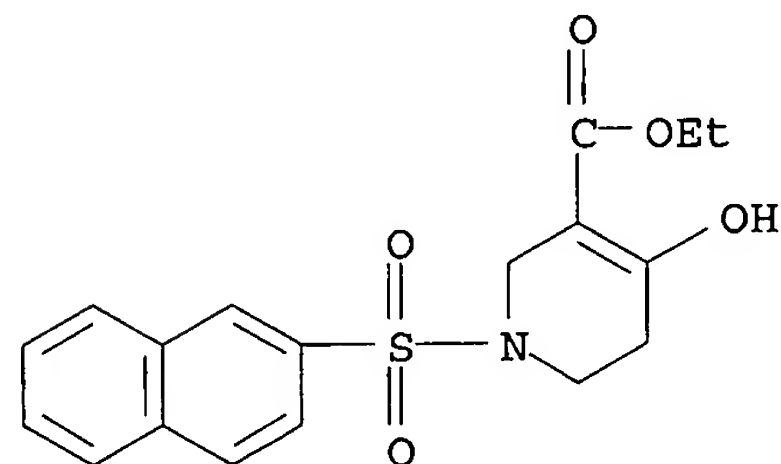
CN Pyrrolidine, 1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-4-[[triphenylmethylthio]methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 393793-61-8 HCAPLUS

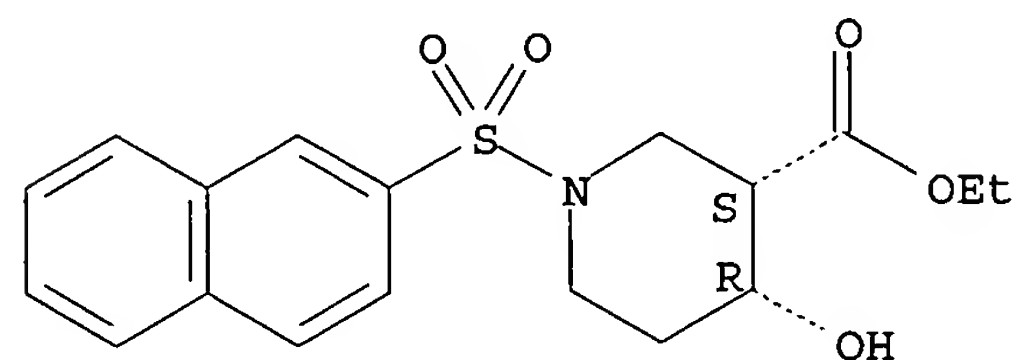
CN 3-Pyridinecarboxylic acid, 1,2,5,6-tetrahydro-4-hydroxy-1-(2-naphthalenylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 393793-63-0 HCAPLUS

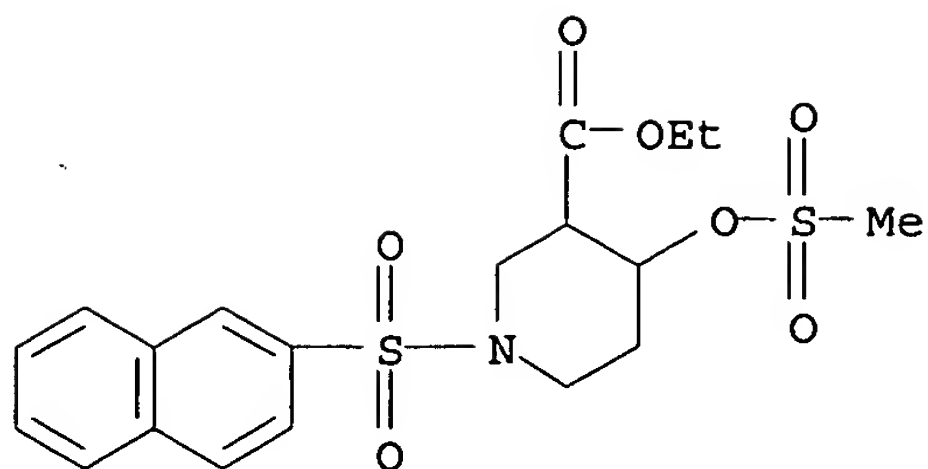
CN 3-Piperidinecarboxylic acid, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, ethyl ester, (3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



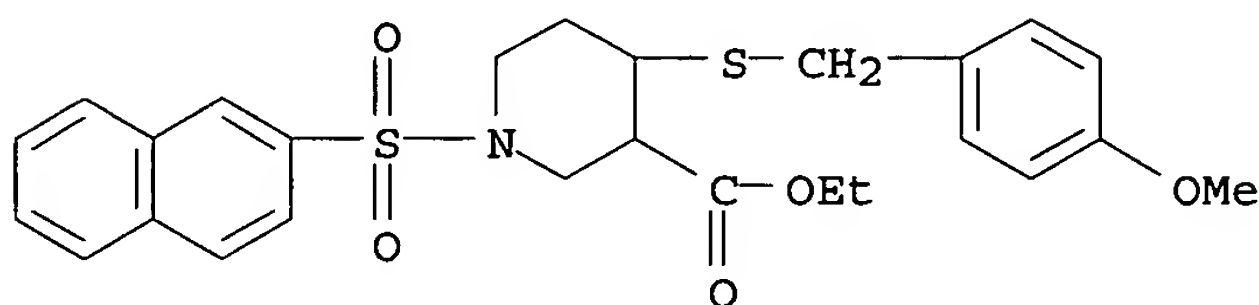
RN 393793-64-1 HCAPLUS

CN 3-Piperidinecarboxylic acid, 4-[(methylsulfonyl)oxy]-1-(2-naphthalenylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 393793-65-2 HCAPLUS

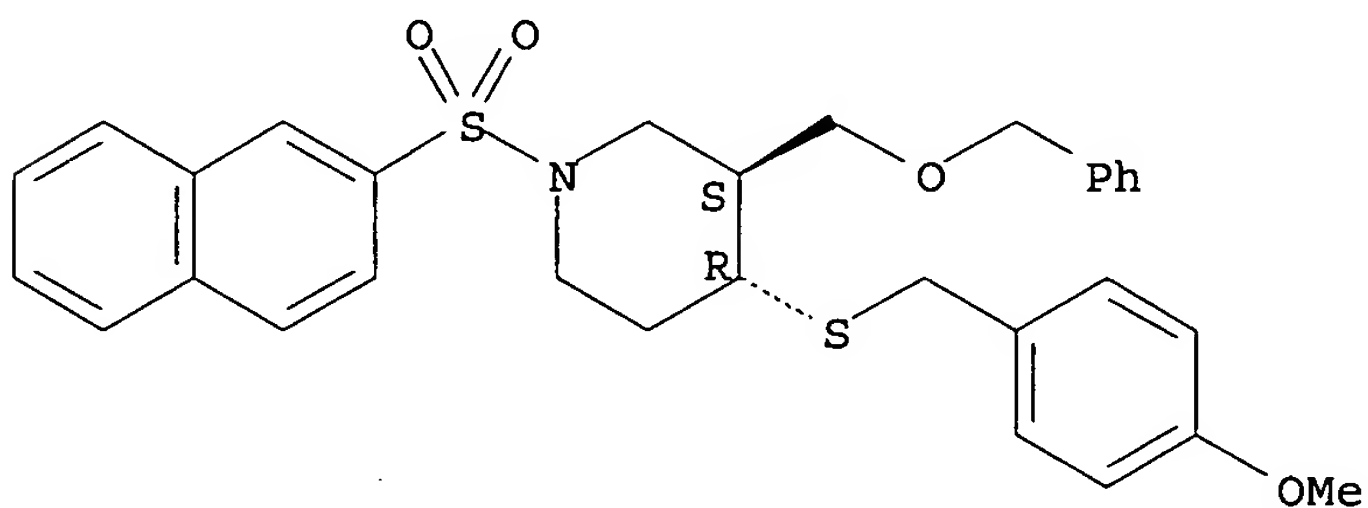
CN 3-Piperidinecarboxylic acid, 4-[[[4-methoxyphenyl]methyl]thio]-1-(2-naphthalenylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 393793-69-6 HCAPLUS

CN Piperidine, 4-[[[4-methoxyphenyl]methyl]thio]-1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-, (3R,4S)-rel- (9CI) (CA INDEX NAME)

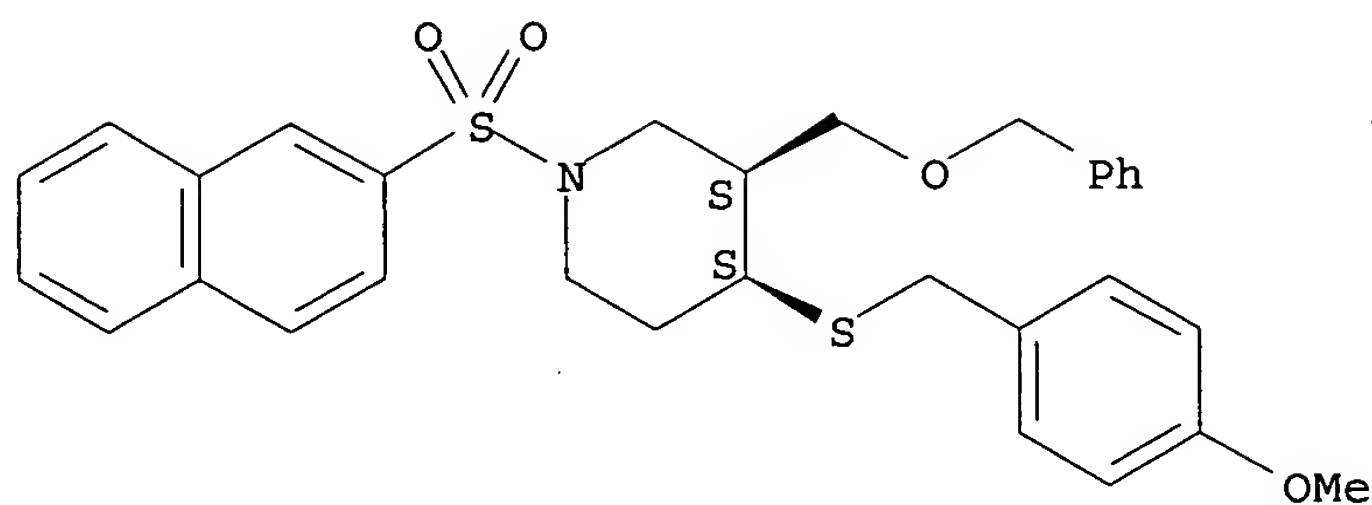
Relative stereochemistry.



RN 393793-70-9 HCAPLUS

CN Piperidine, 4-[[[4-methoxyphenyl]methyl]thio]-1-(2-naphthalenylsulfonyl)-3-[(phenylmethoxy)methyl]-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

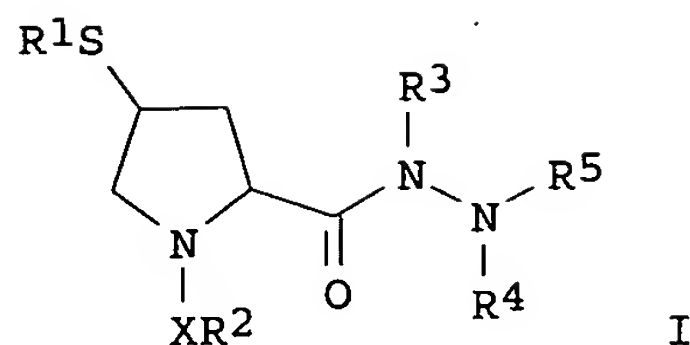
Relative stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:72039 HCAPLUS  
 DOCUMENT NUMBER: 136:118380  
 TITLE: Pyrrolidine-2-carboxylic acid hydrazide derivatives  
 for use as metalloprotease inhibitors  
 INVENTOR(S): Aebi, Johannes; Dehmlow, Henrietta; Kitas, Eric  
 Argirios  
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 78 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: **Patent**  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006224	A1	20020124	WO 2001-EP7995	20010711 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002040048	A1	20020404	US 2001-900350	20010706 <--
US 6444829	B2	20020903		
CA 2415665	AA	20020124	CA 2001-2415665	20010711 <--
EP 1317428	A1	20030611	EP 2001-954031	20010711 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012543	A	20030701	BR 2001-12543	20010711 <--
JP 2004504298	T2	20040212	JP 2002-512130	20010711
ZA 2003000172	A	20040407	ZA 2003-172	20030107
PRIORITY APPLN. INFO.:			EP 2000-114948	A 20000719
			WO 2001-EP7995	W 20010711
OTHER SOURCE(S):	MARPAT 136:118380			
GI				



AB Title compds. I [R1 = H, acyl; R2 = (un)substituted alkyl, cycloalkyl, akynyl, aryl, heterocyclic; R3 = H, aryl, alkyl, aralkyl, arylsulfonyl, heteroarylsulfonyl; R4 = H, aralkyl, alkyl, aryl, cycloalkyl, cycloalkylalkyl, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, heteroarylsulfonyl, carboxyalkyl, carboxyalkylsulfonyl, alkoxyalkyl; NR4R5, R3NNR4R5 = heterocyclic; R5 = H, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, acyl, heterocyclyl, (un)substituted aminosulfonyl, aminoalkylcarbonyl, arylcarbonyl, alkyl, acyl, alkoxyalkyl, aryl, aralkyl, arylalkoxyalkyl, heteroaryl; X = SO2, SO2NH, CO, (un)substituted CONH, CO2] were prepared for use as inhibitors of metalloproteases, e.g. zinc proteases, particularly zinc hydrolases, and are effective in treating disease states associated with vasoconstriction of increasing occurrences. Thus, (2S,4R)-I [X = SO2, R1, R3 = H, R2 = 2-naphthyl, NR4R5 = 2-oxopyrrolidino] was prepared from L-hydroxyproline Me ester hydrochloride in 7 steps.

IT 391671-83-3P 391671-85-5P 391671-90-2P  
391671-92-4P 391672-17-6P 391672-19-8P  
391672-22-3P 391673-01-1P

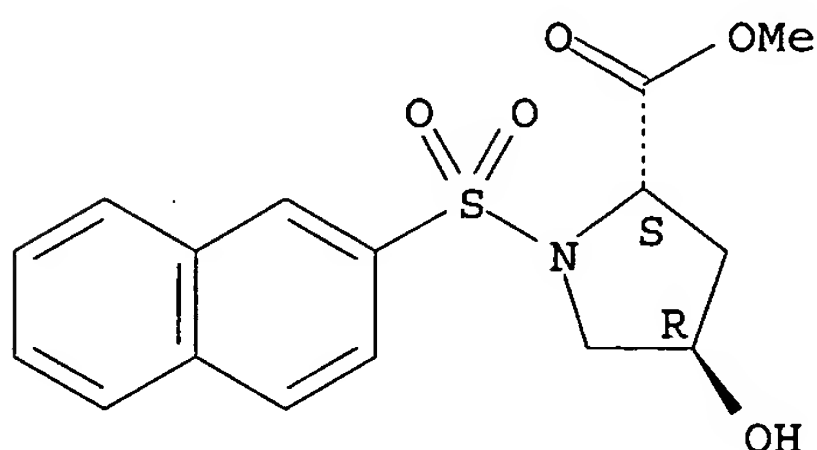
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrrolidine-2-carboxylic acid hydrazide derivs. for use as metalloprotease inhibitors)

RN 391671-83-3 HCAPLUS

CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

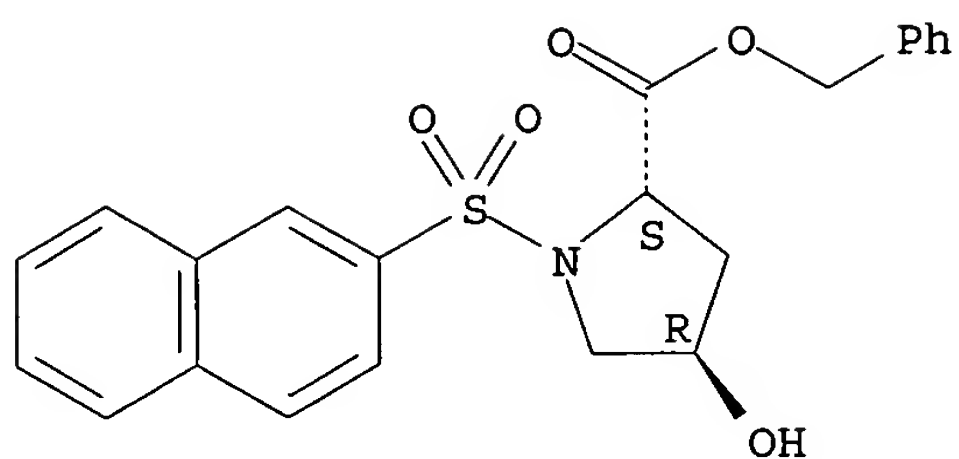
Absolute stereochemistry.



RN 391671-85-5 HCAPLUS

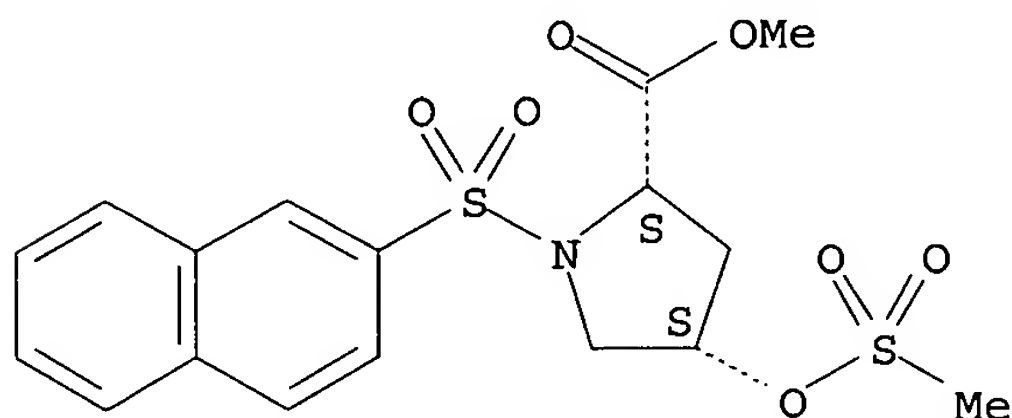
CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



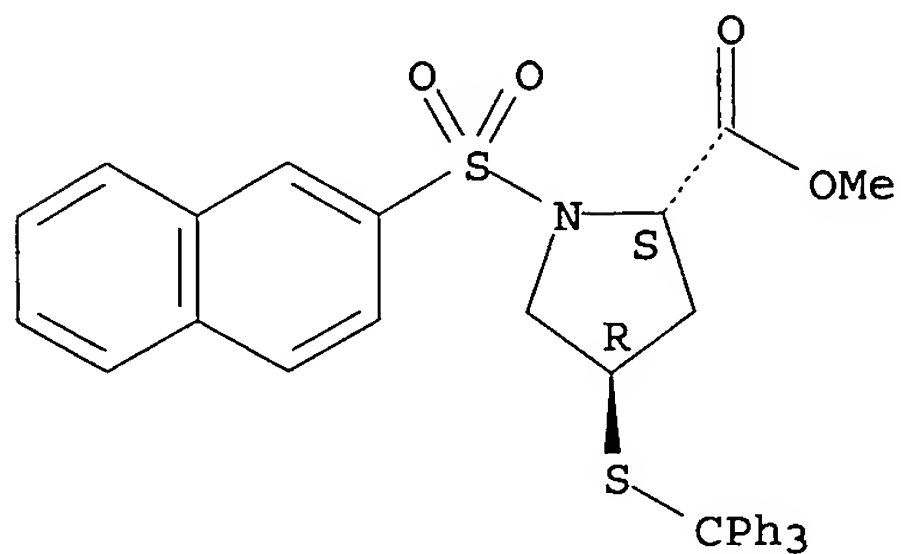
RN 391671-90-2 HCAPLUS  
 CN L-Proline, 4-[(methoxycarbonyloxy)-1-(2-naphthalenylsulfonyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 391671-92-4 HCAPLUS  
 CN L-Proline, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

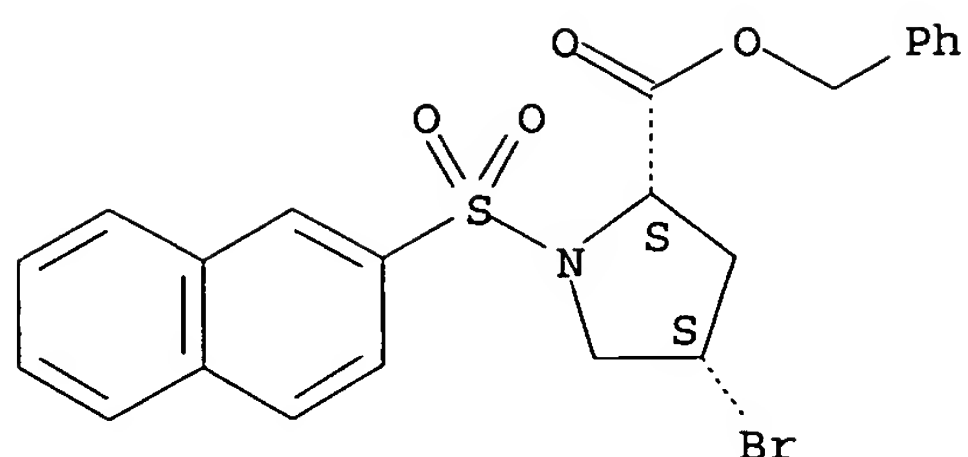
Absolute stereochemistry.



RN 391672-17-6 HCAPLUS  
 CN L-Proline, 4-bromo-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

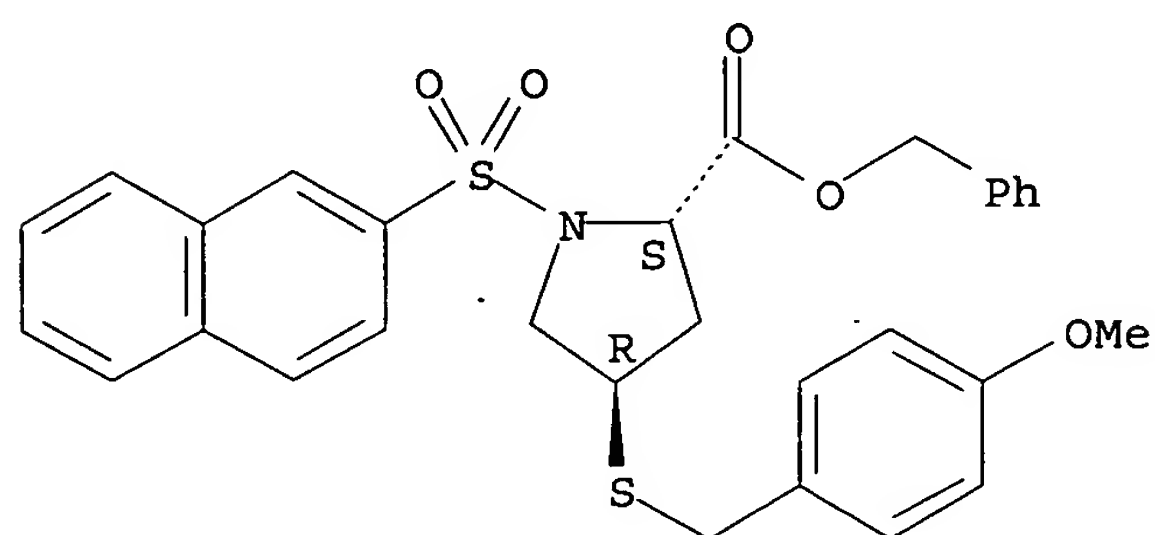




RN 391672-19-8 HCAPLUS

CN L-Proline, 4-[[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)- (9CI) (CA INDEX NAME)

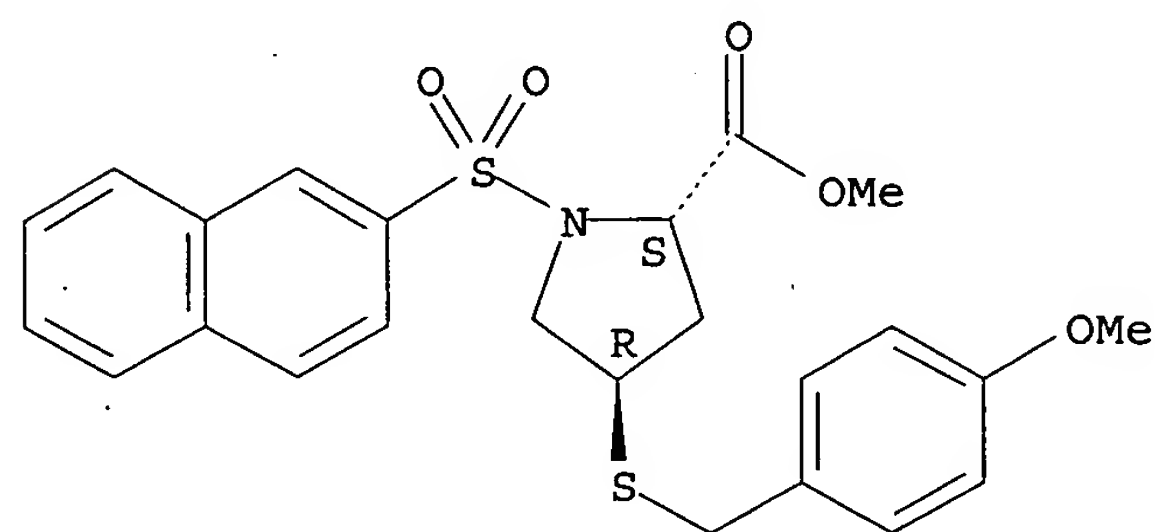
Absolute stereochemistry.



RN 391672-22-3 HCAPLUS

CN L-Proline, 4-[[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

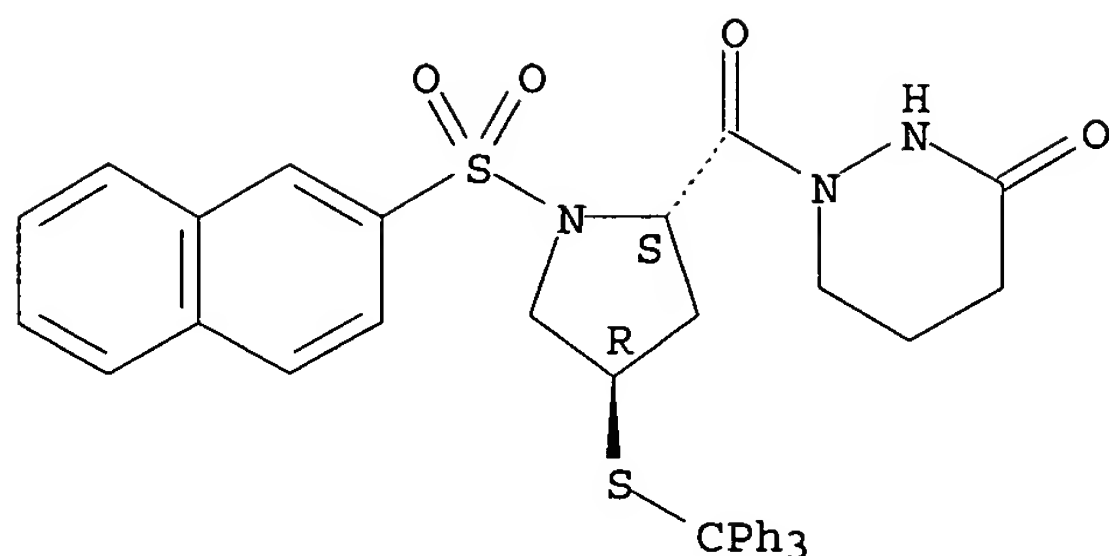
Absolute stereochemistry.



RN 391673-01-1 HCAPLUS

CN 3(2H)-Pyridazinone, tetrahydro-1-[[[(2S,4R)-1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 391673-03-3P 391673-66-8P

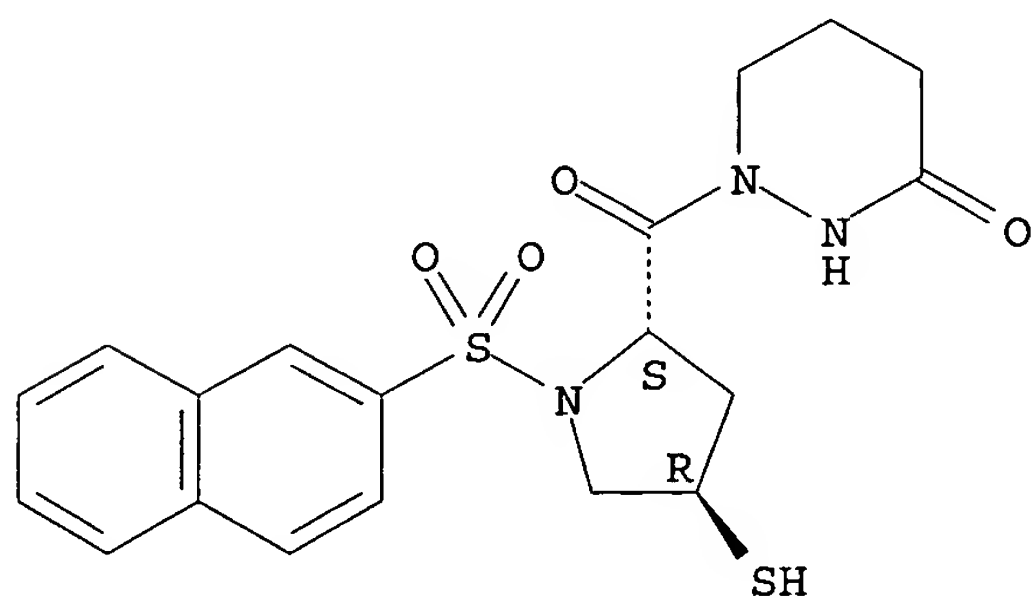
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrrolidine-2-carboxylic acid hydrazide derivs. for use as metalloprotease inhibitors)

RN 391673-03-3 HCAPLUS

CN 3(2H)-Pyridazinone, tetrahydro-1-[[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

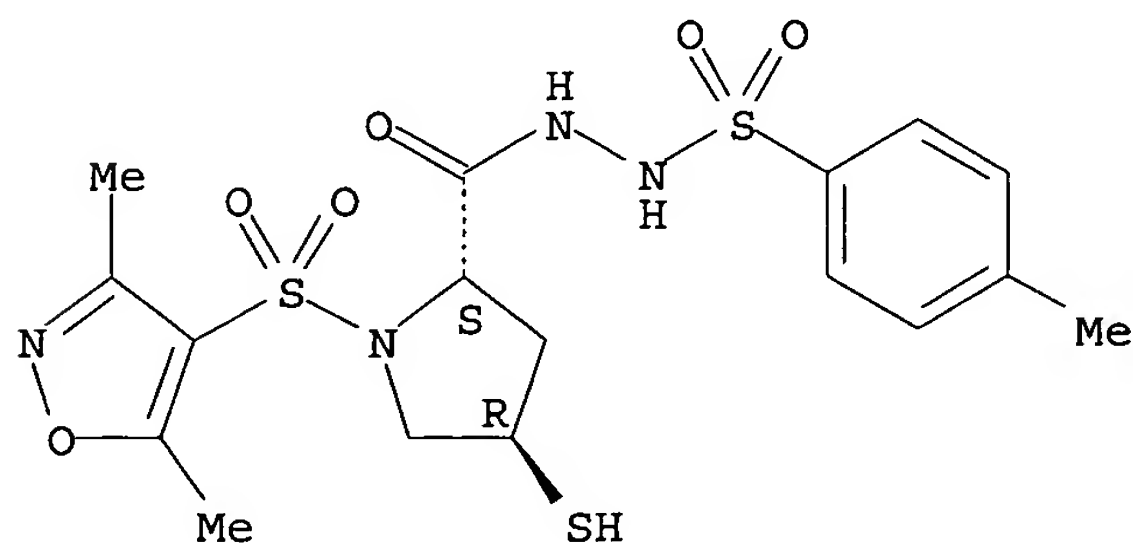
Absolute stereochemistry.



RN 391673-66-8 HCAPLUS

CN L-Proline, 1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-4-mercapto-, 2-[(4-methylphenyl)sulfonyl]hydrazide, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:72037 HCAPLUS

DOCUMENT NUMBER: 136:134667

TITLE: Preparation of mercaptopyrrolidinecarboxamides related compounds as **inhibitors** of endothelin-converting **enzyme**

INVENTOR(S): Aebi, Johannes; Blum, Denise; Bur, Daniel; Chucholowski, Alexander; Dehmlow, Henrietta; Kitas, Eric Argirios; Loeffler, Bernd Michael; Obst, Ulrike; Wallbaum, Sabine

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 160 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

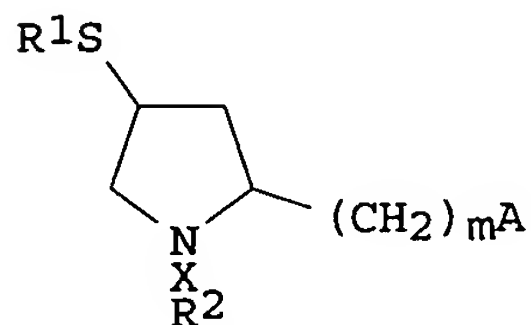
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006222	A1	20020124	WO 2001-EP7950	20010710 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2414311	AA	20020124	CA 2001-2414311	20010710 <--
EP 1303485	A1	20030423	EP 2001-949485	20010710 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012580	A	20030617	BR 2001-12580	20010710 <--
JP 2004504297	T2	20040212	JP 2002-512128	20010710
US 2002049243	A1	20020425	US 2001-907135	20010717 <--
US 6541638	B2	20030401		
ZA 2003000167	A	20040407	ZA 2003-167	20030107
PRIORITY APPLN. INFO.:			EP 2000-114947	A 20000719
			WO 2001-EP7950	W 20010710

OTHER SOURCE(S): MARPAT 136:134667

GI



I

AB Title compds. [I; R<sub>1</sub> = H, alkylcarbonyl, arylcarbonyl; R<sub>2</sub> = alkyl, alkylcycloalkyl, cycloalkyl, haloalkyl, carboxyalkyl, aryl, alkynyl, aryloxyalkyl, heterocyclyl, etc.; A = COR<sub>3</sub>, CH(OH)R<sub>4</sub>, CONR<sub>5</sub>R<sub>6</sub>; R<sub>3</sub>, R<sub>4</sub> = alkyl, aryl, arylalkynyl, aralkyl, arylalkenyl; R<sub>5</sub> = H, alkyl, cycloalkyl,

cycloalkylalkyl, carboxyalkyl, aralkyl; R6 = alkyl, alkylcarbonylalkyl, cyanoalkyl, hydroxyalkyl, aminocarbonylalkyl, aryl, etc.; m = 0-2; X = SO<sub>2</sub>, CO, CO<sub>2</sub>, SO<sub>2</sub>NH, CONR<sub>13</sub>; R<sub>13</sub> = H, alkyl, aryl, carboxyalkyl, and dimers thereof, were prepared. Thus, (2S,4R)-[[4-(4-methoxybenzylsulfanyl)-1-(naphthalene-2-sulfonyl)pyrrolidine-2-carbonyl]methylamino]acetic acid (preparation given) in CH<sub>2</sub>Cl<sub>2</sub> were treated with NMM, HOBT in CH<sub>2</sub>Cl<sub>2</sub>, EDCI in CH<sub>2</sub>Cl<sub>2</sub>, and o-toluidine in CH<sub>2</sub>Cl<sub>2</sub>; the solution was shaken overnight to give a residue which was treated with Et<sub>3</sub>SiH in CF<sub>3</sub>CO<sub>2</sub>H at 80° for 1 h to give (2S,4R)-4-mercapto-1-(naphthalene-2-sulfonyl)pyrrolidine-2-carboxylic acid methyl(o-tolylcarbamoylmethyl)amide. I inhibited endothelin converting **enzyme** with IC<sub>50</sub> = 5-1000 nM.

IT 393153-57-6P 393153-58-7P 393153-78-1P  
 393156-50-8P 393156-51-9P 393156-52-0P  
 393156-53-1P 393157-03-4P 393157-08-9P  
 393157-26-1P 393157-30-7P 393157-31-8P  
 393157-60-3P 393157-62-5P 393157-71-6P  
 393157-75-0P 393157-79-4P 393157-82-9P  
 393158-73-1P 393158-74-2P 393158-75-3P  
 393158-76-4P 393159-15-4P 393159-18-7P

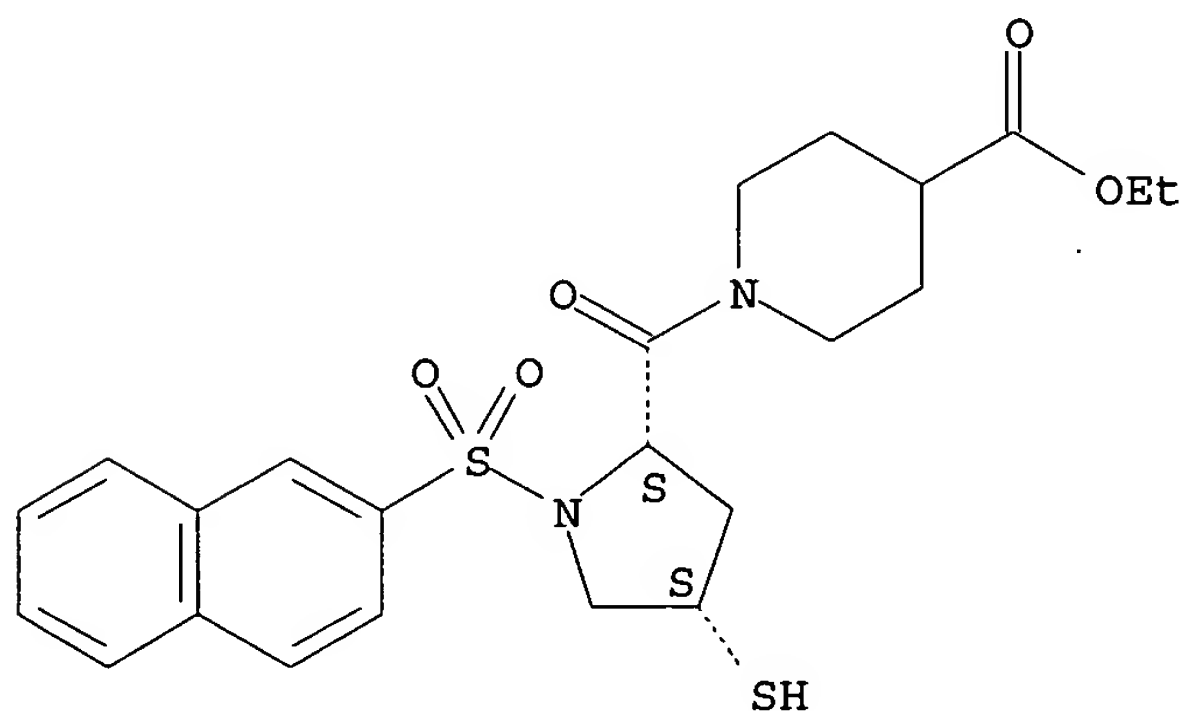
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of mercaptopyrrolidinecarboxamides as **inhibitors** of endothelin-converting **enzyme**)

RN 393153-57-6 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

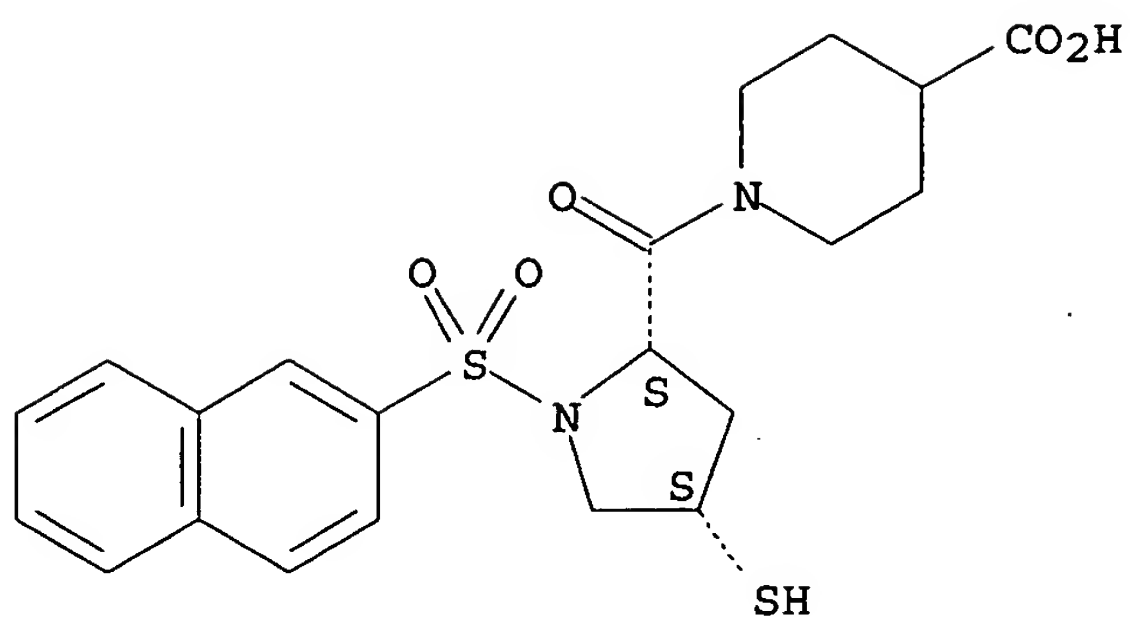
Absolute stereochemistry.



RN 393153-58-7 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

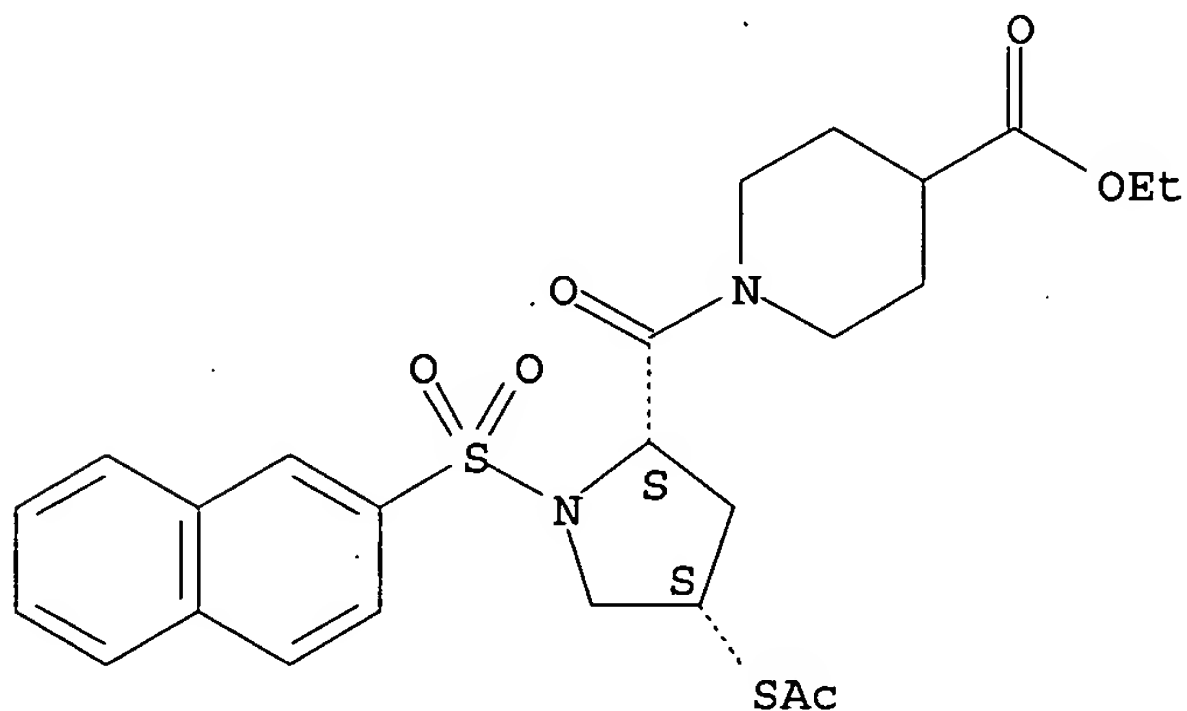
Absolute stereochemistry.



RN 393153-78-1 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-(acetylthio)-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

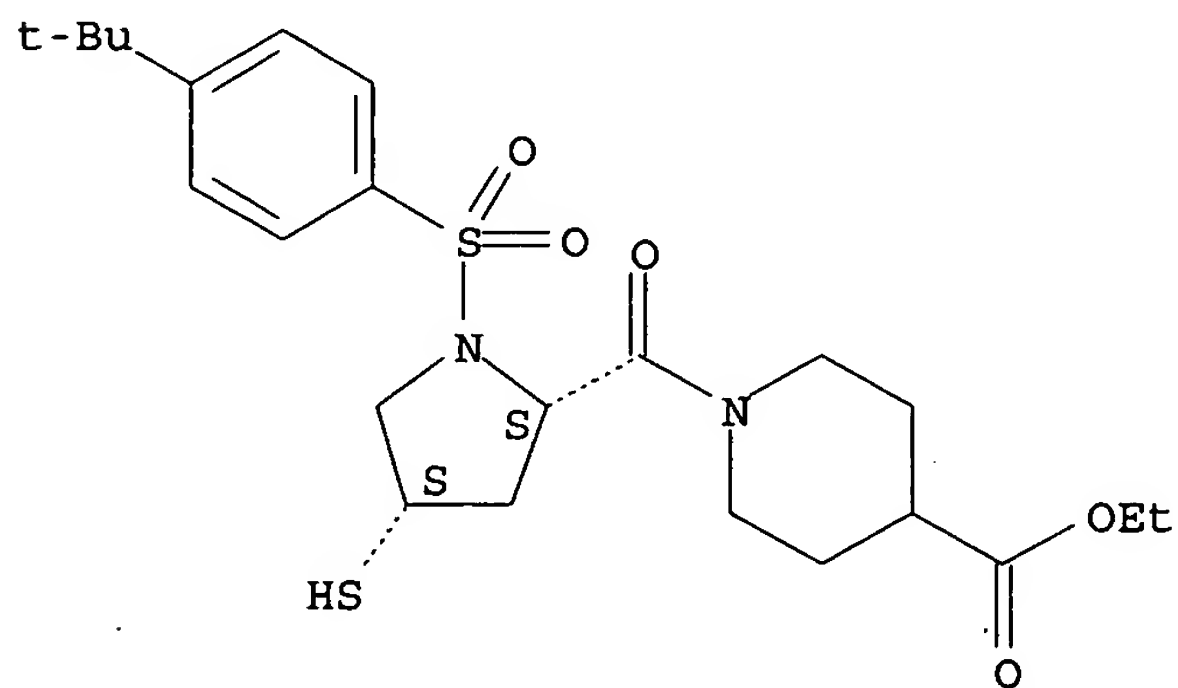
Absolute stereochemistry.



RN 393156-50-8 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

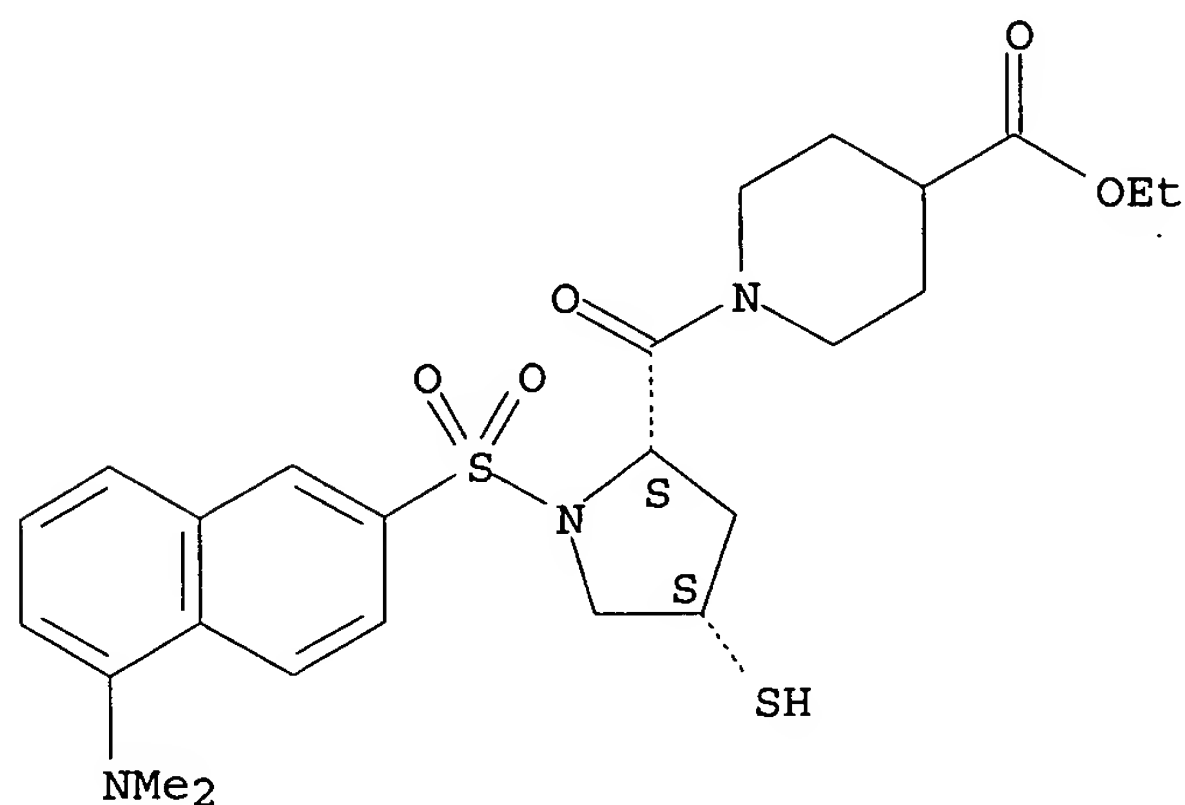
Absolute stereochemistry.



RN 393156-51-9 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-1-[[5-(dimethylamino)-2-naphthalenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

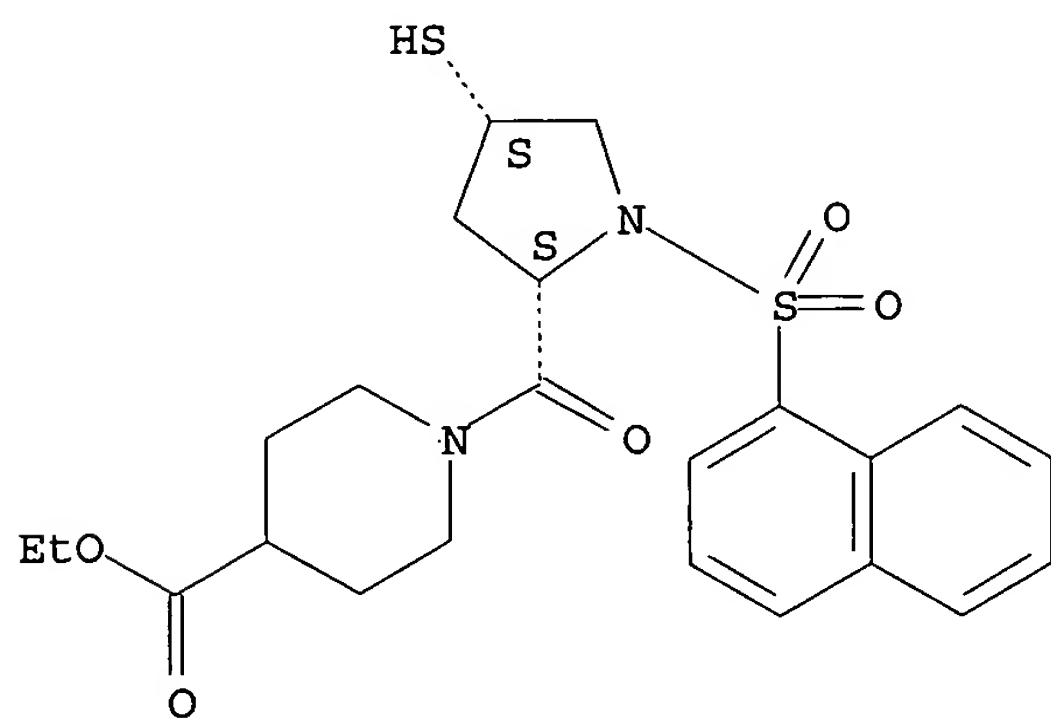
Absolute stereochemistry.



RN 393156-52-0 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-(1-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

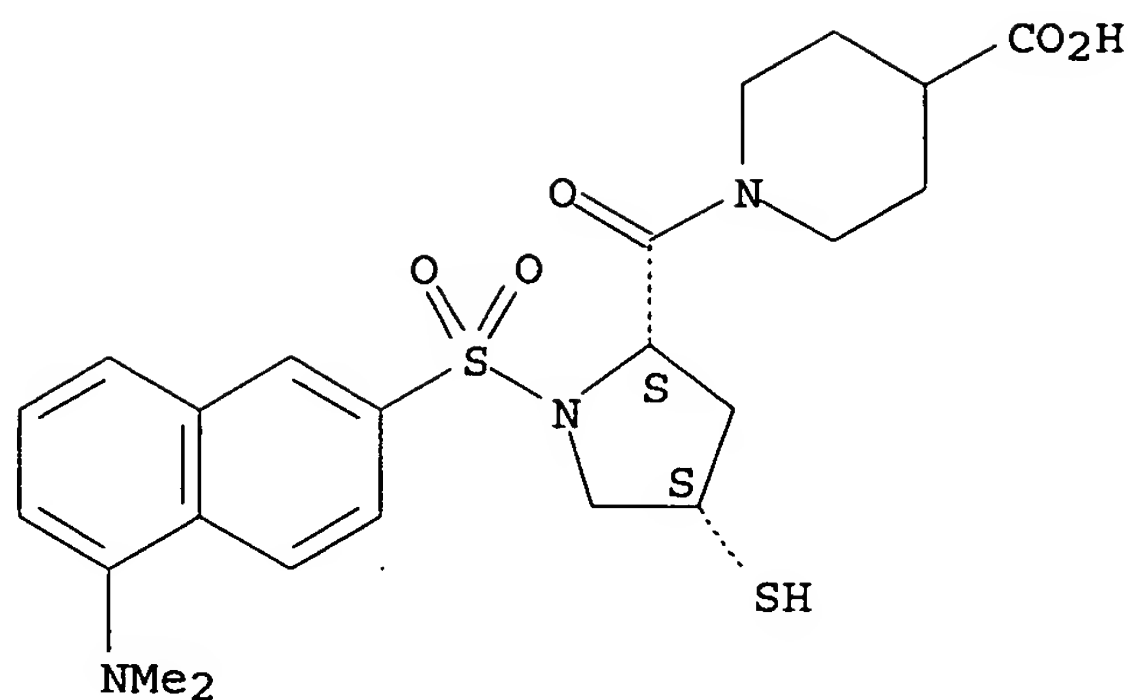
Absolute stereochemistry.



RN 393156-53-1 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-1-[[5-(dimethylamino)-2-naphthalenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

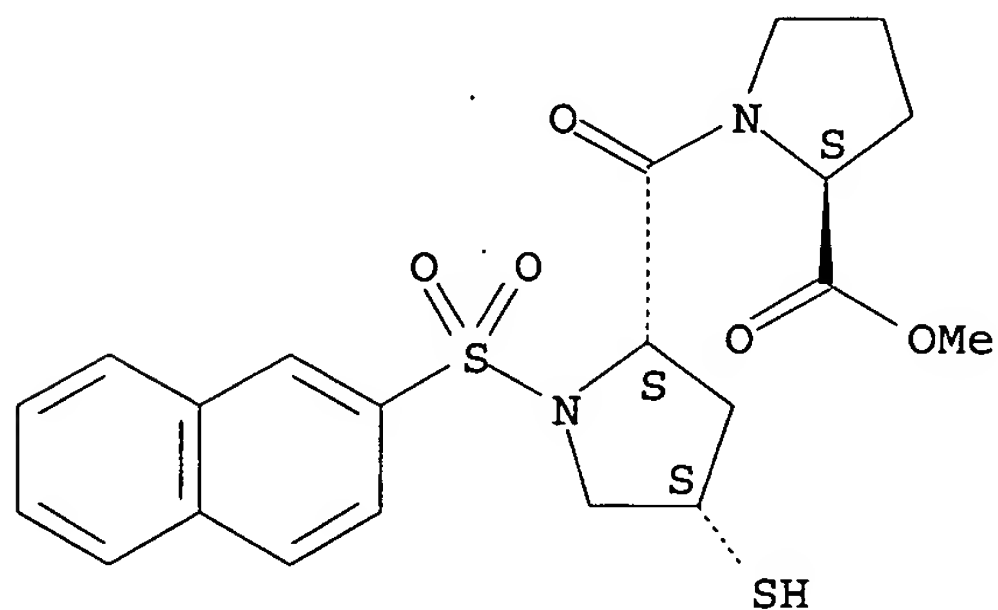
Absolute stereochemistry.



RN 393157-03-4 HCAPLUS

CN L-Proline, (4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-, methyl ester (9CI) (CA INDEX NAME)

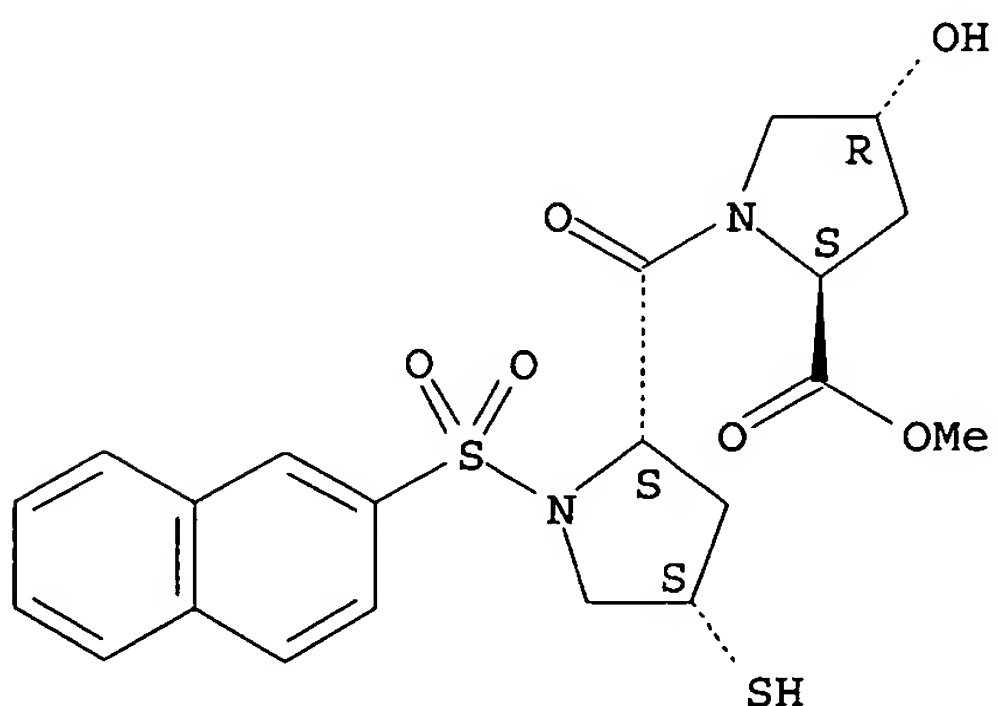
Absolute stereochemistry.



RN 393157-08-9 HCAPLUS

CN L-Proline, (4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-4-hydroxy-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

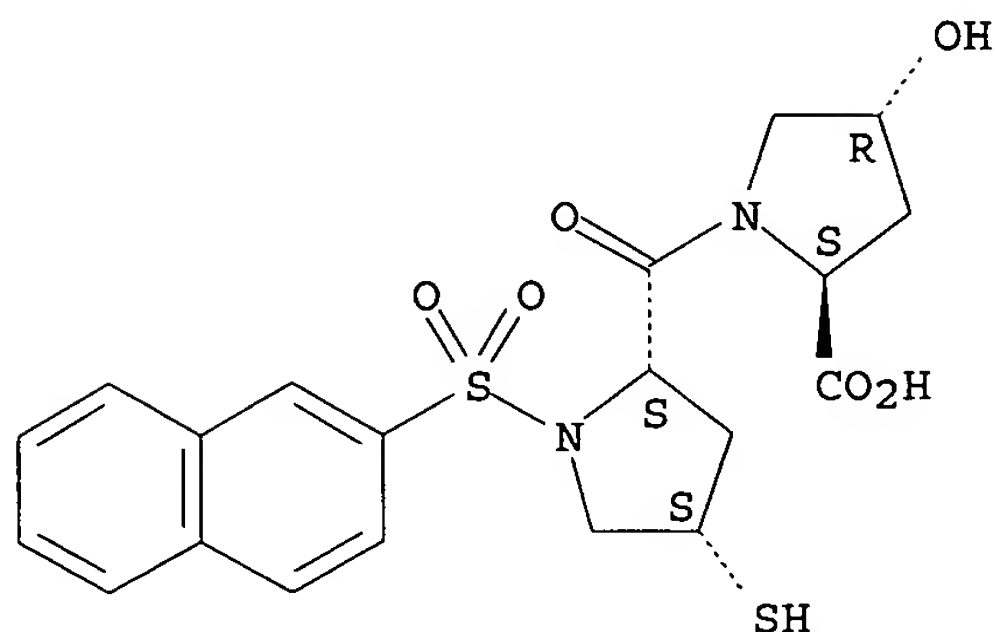


RN 393157-26-1 HCAPLUS

CN L-Proline, (4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-4-hydroxy-,

(4R) - (9CI) (CA INDEX NAME)

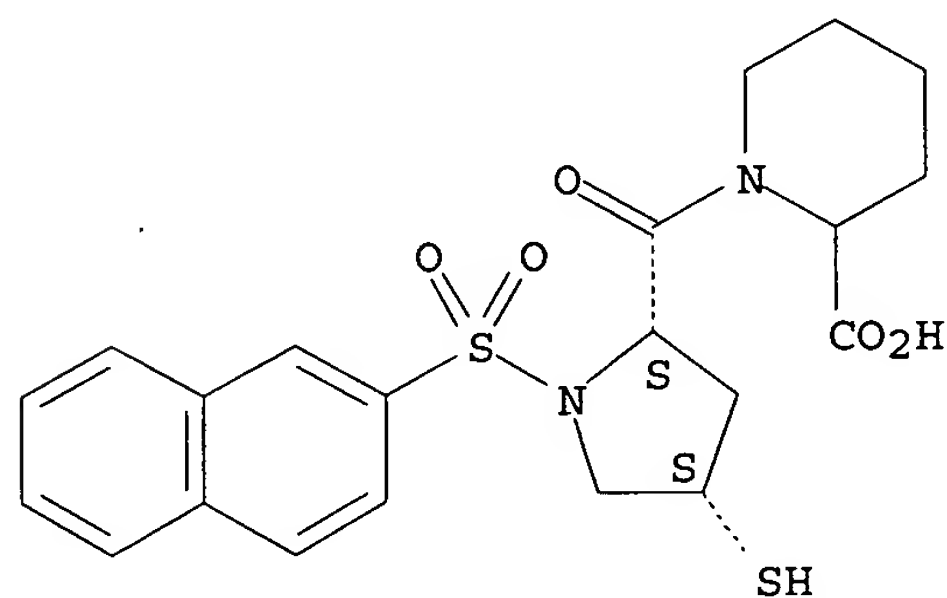
Absolute stereochemistry.



RN 393157-30-7 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

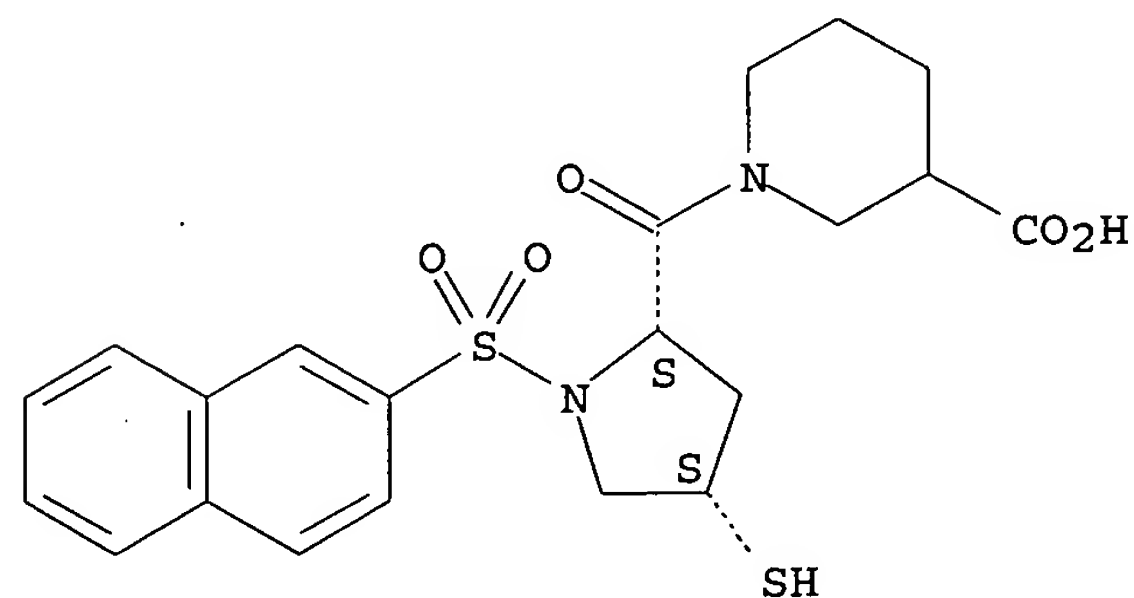
Absolute stereochemistry.



RN 393157-31-8 HCAPLUS

CN 3-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



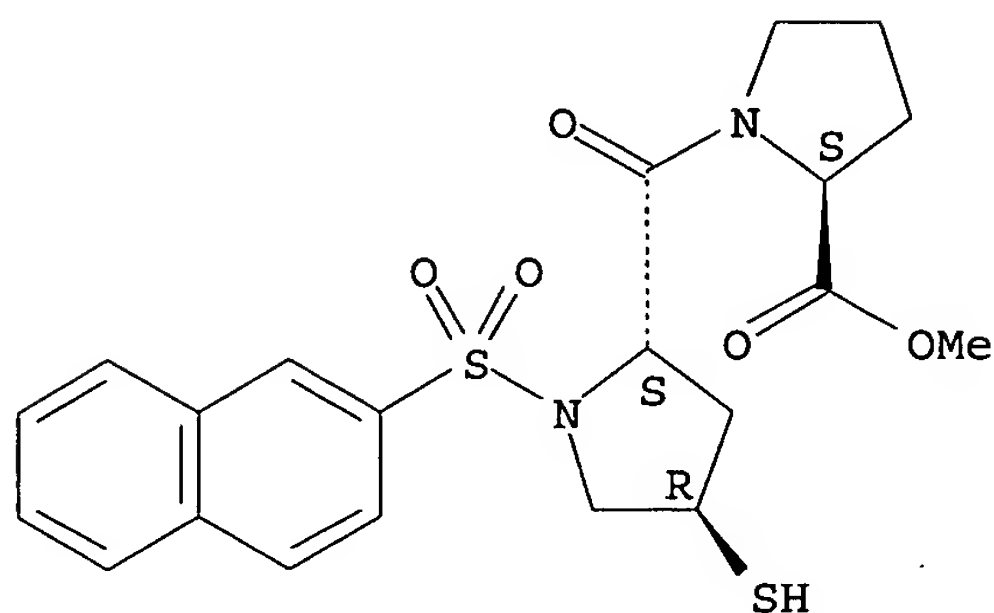
RN 393157-60-3 HCAPLUS

CN L-Proline, (4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-, methyl



ester (9CI) (CA INDEX NAME)

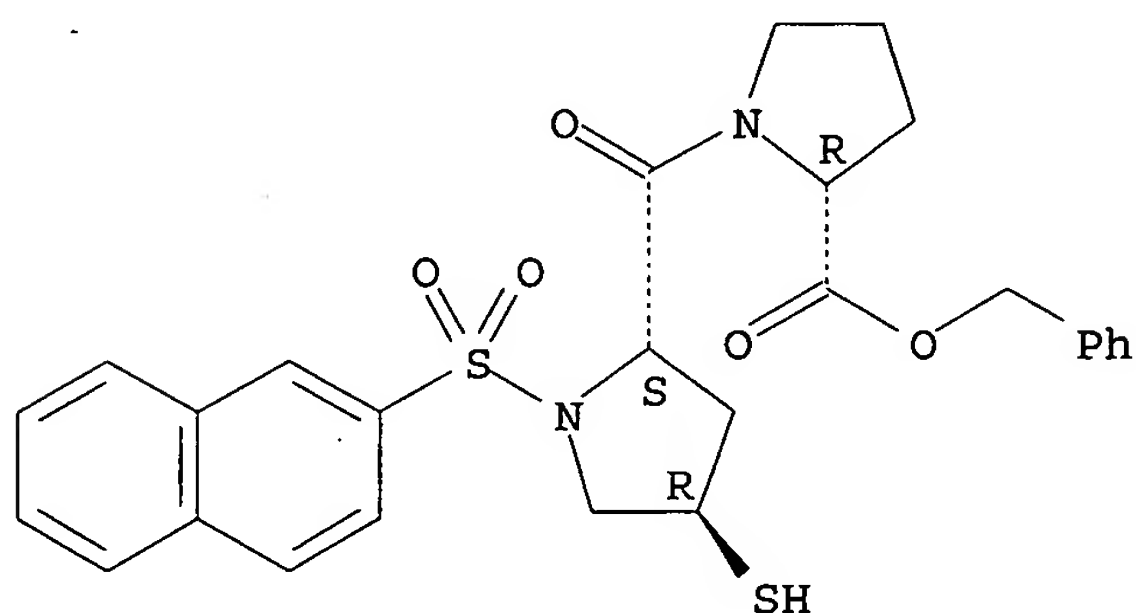
Absolute stereochemistry.



RN 393157-62-5 HCAPLUS

CN D-Proline, (4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

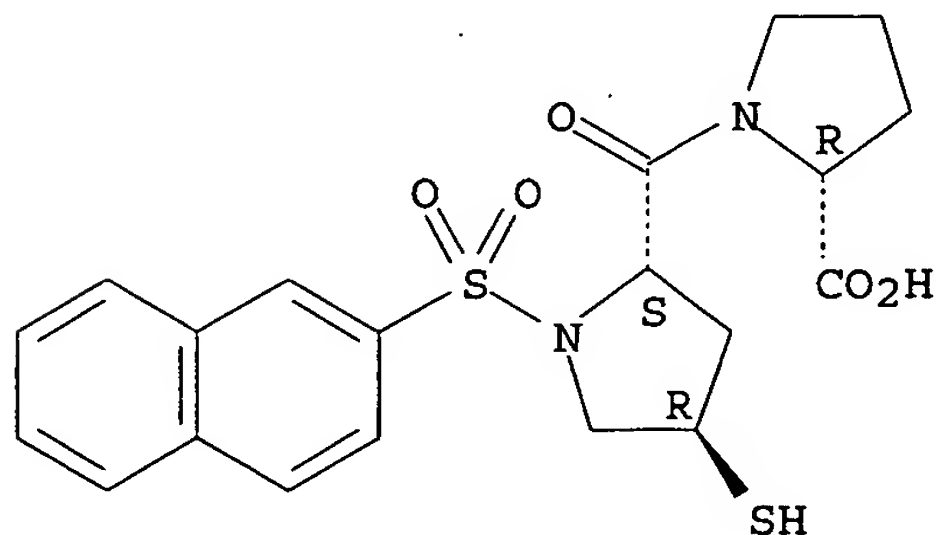
Absolute stereochemistry.



RN 393157-71-6 HCAPLUS

CN D-Proline, (4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl- (9CI) (CA INDEX NAME)

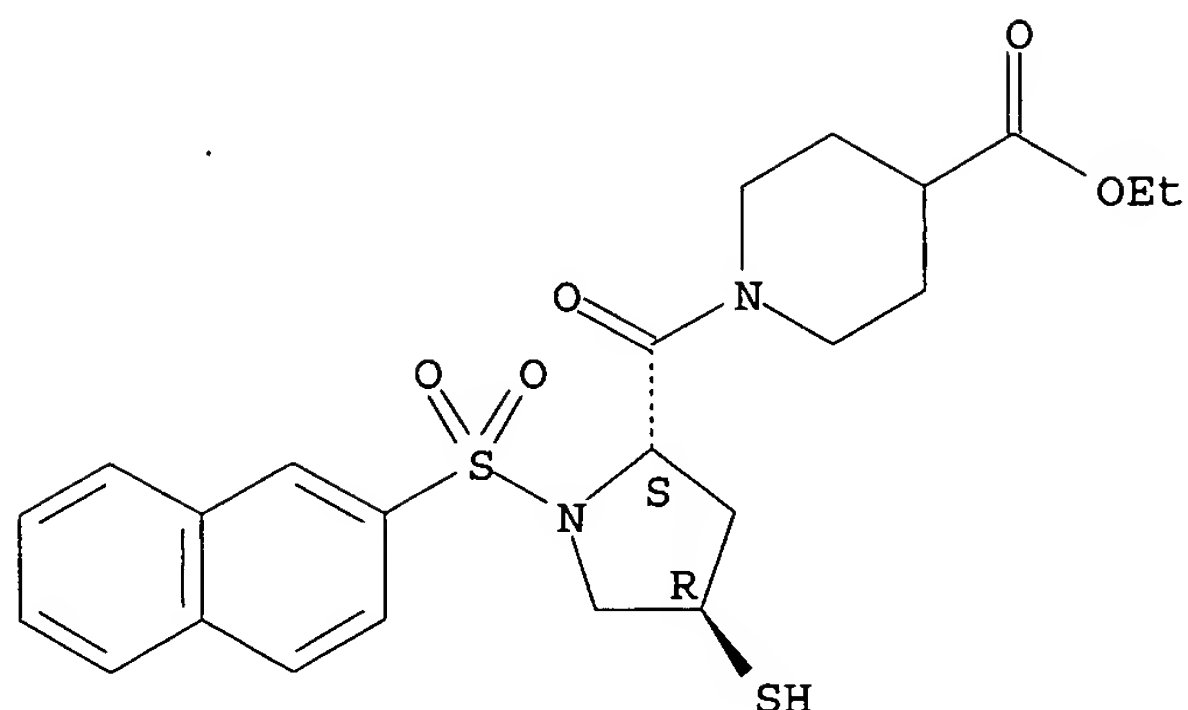
Absolute stereochemistry.



RN 393157-75-0 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

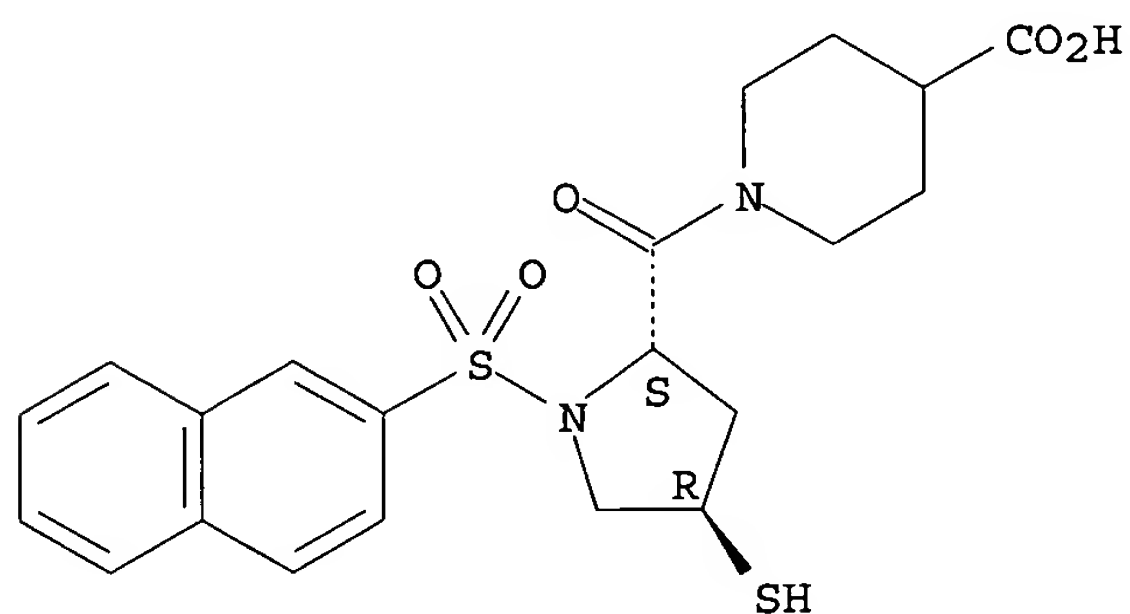
Absolute stereochemistry.



RN 393157-79-4 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4R)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

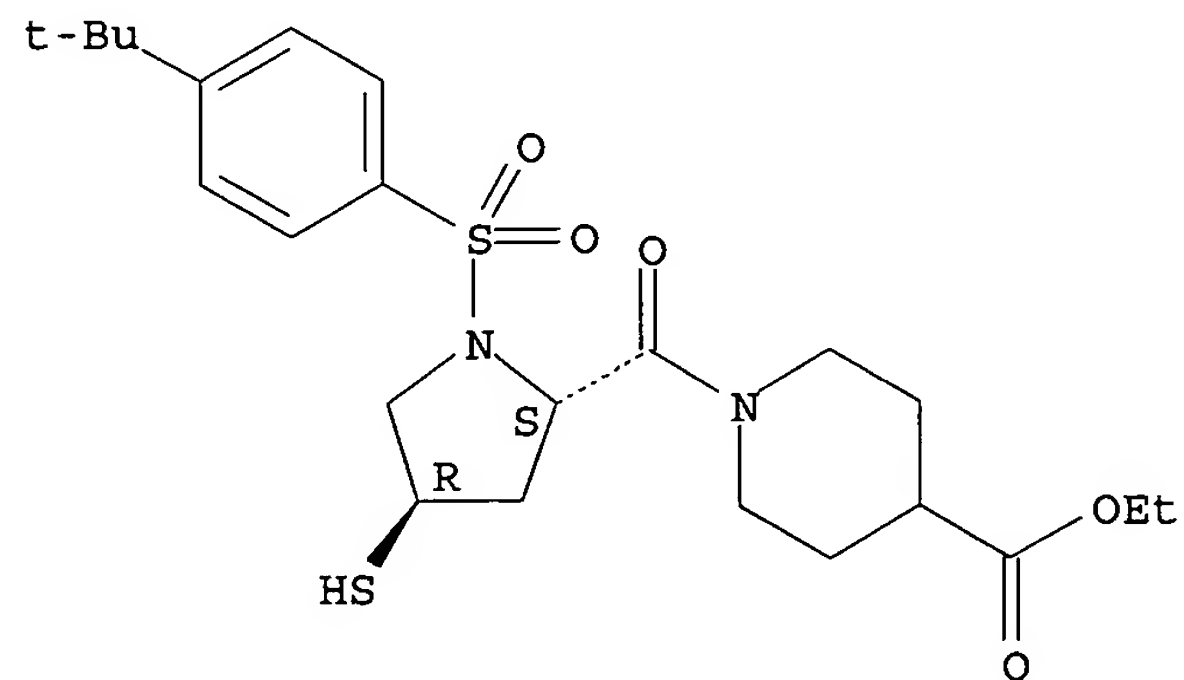
Absolute stereochemistry.



RN 393157-82-9 HCAPLUS

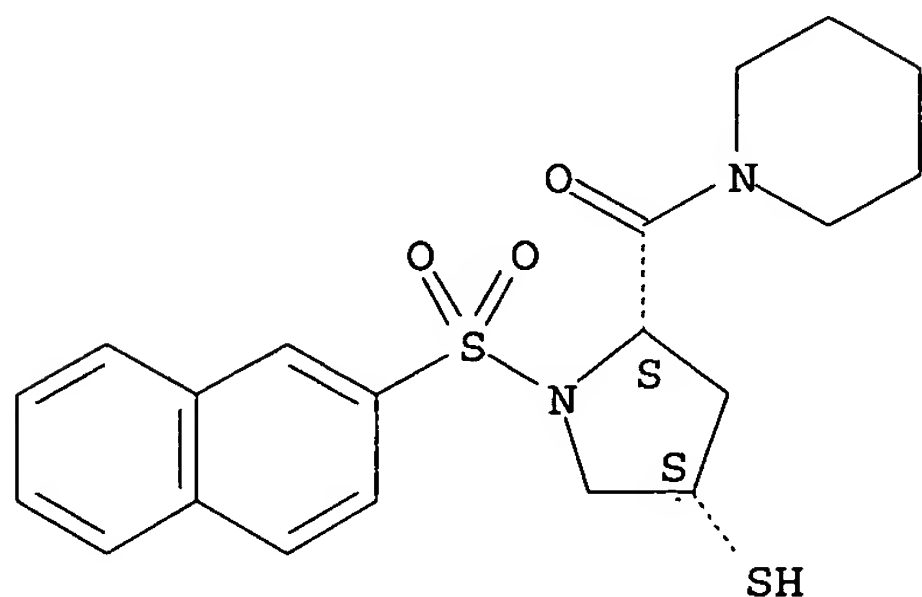
CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4R)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



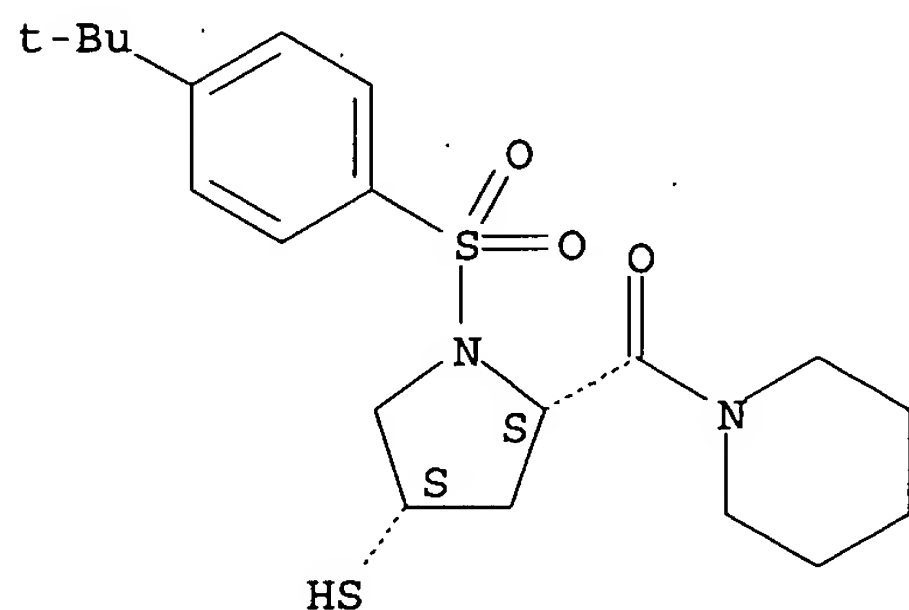
RN 393158-73-1 HCAPLUS  
 CN Piperidine, 1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



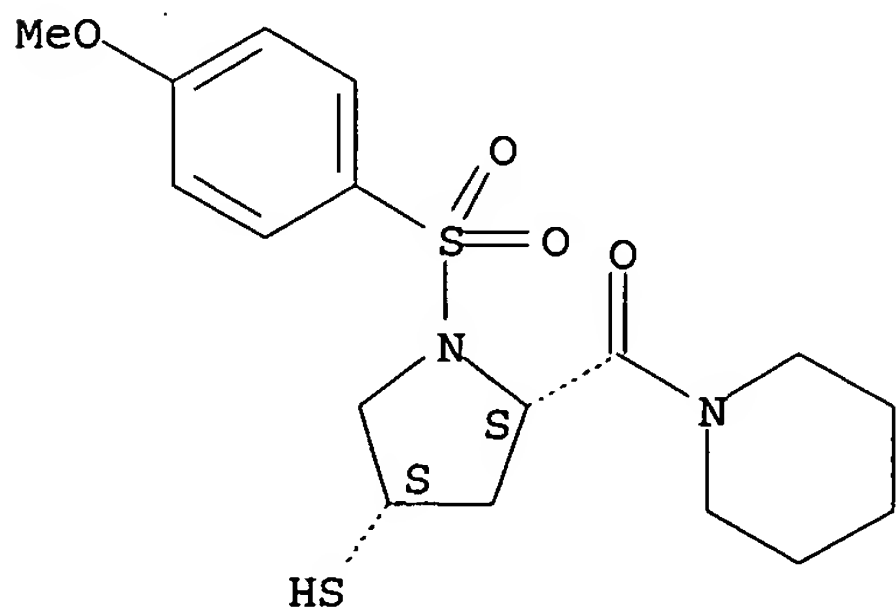
RN 393158-74-2 HCAPLUS  
 CN Piperidine, 1-[[[(2S,4S)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393158-75-3 HCAPLUS  
 CN Piperidine, 1-[[[(2S,4S)-4-mercapto-1-[(4-methoxyphenyl)sulfonyl]-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

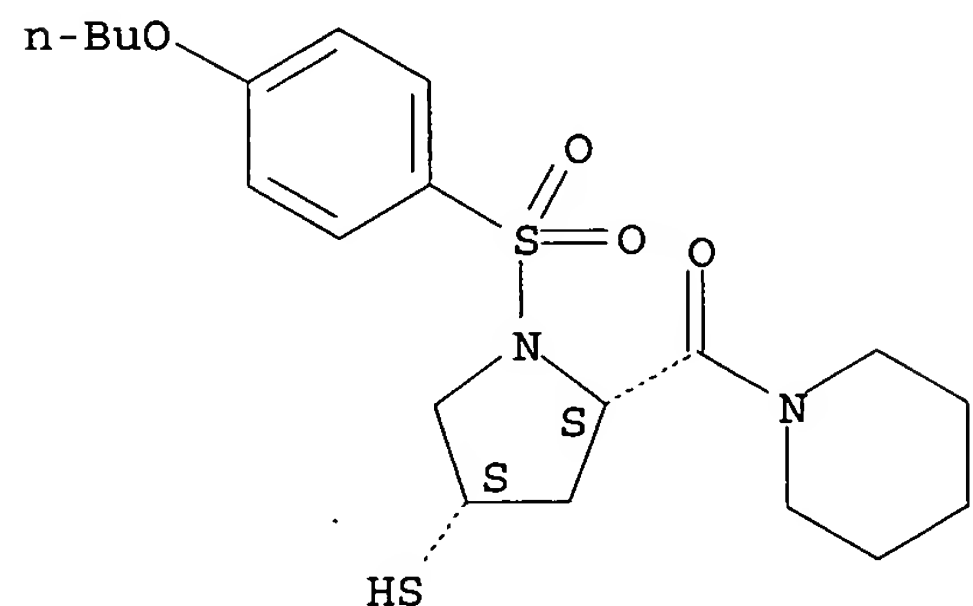
Absolute stereochemistry.



RN 393158-76-4 HCAPLUS

CN Piperidine, 1-[[[(2S,4S)-1-[(4-butoxyphenyl)sulfonyl]-4-mercapto-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

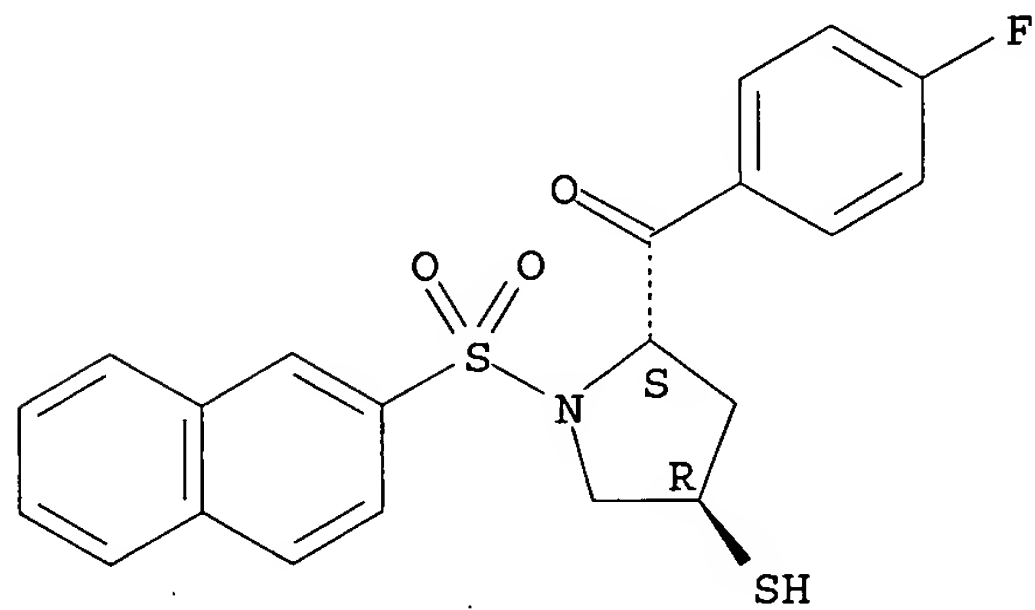
Absolute stereochemistry.



RN 393159-15-4 HCAPLUS

CN 3-Pyrrolidinethiol, 5-(4-fluorobenzoyl)-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

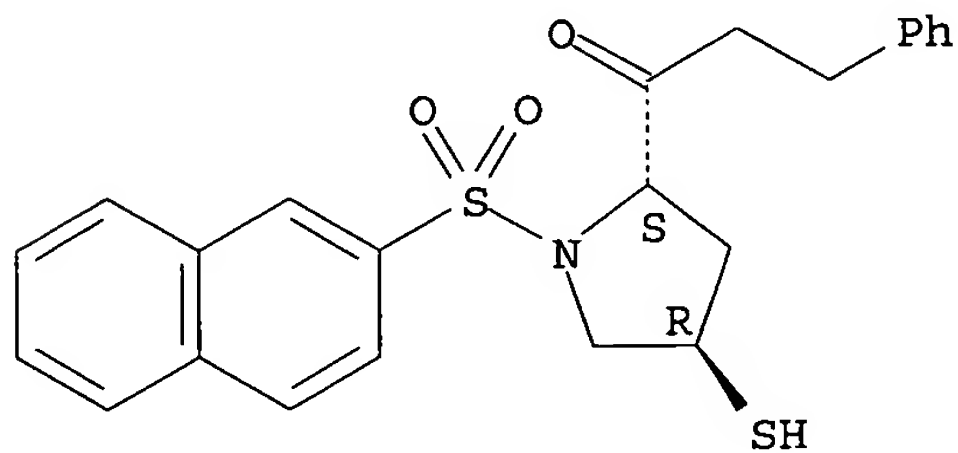
Absolute stereochemistry.



RN 393159-18-7 HCAPLUS

CN 3-Pyrrolidinethiol, 1-(2-naphthalenylsulfonyl)-5-(1-oxo-3-phenylpropyl)-, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 393156-81-5 393156-83-7 393157-14-7

393157-15-8 393157-17-0 393157-18-1

393157-23-8

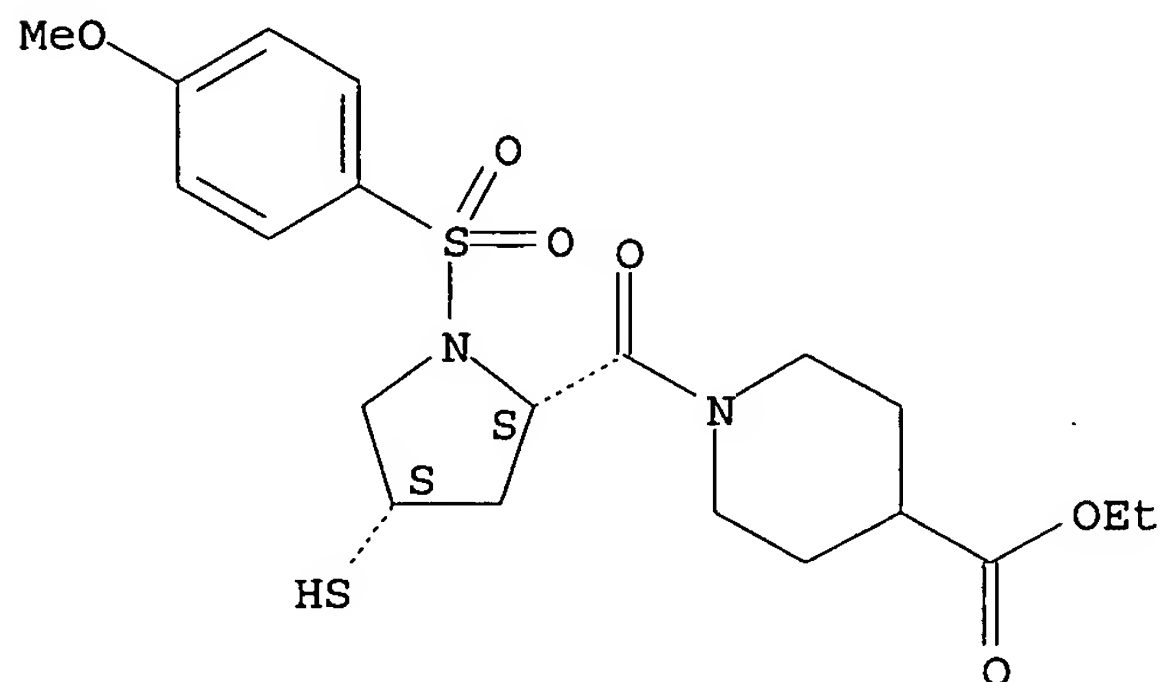
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of mercaptopyrrolidinecarboxamides as inhibitors of endothelin-converting enzyme)

RN 393156-81-5 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-[(4-methoxyphenyl)sulfonyl]-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

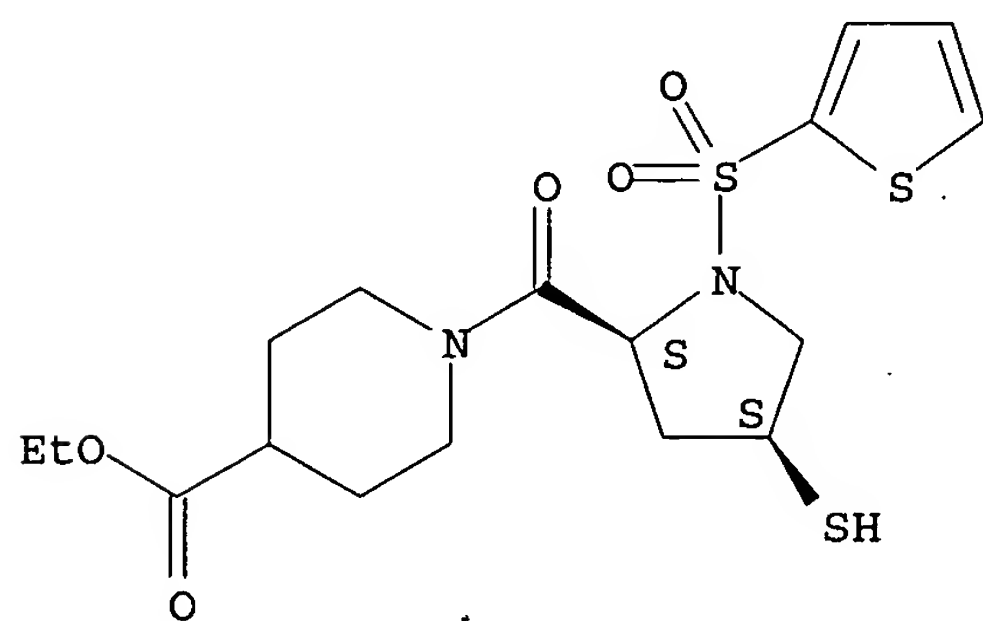
Absolute stereochemistry.



RN 393156-83-7 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-(2-thienylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

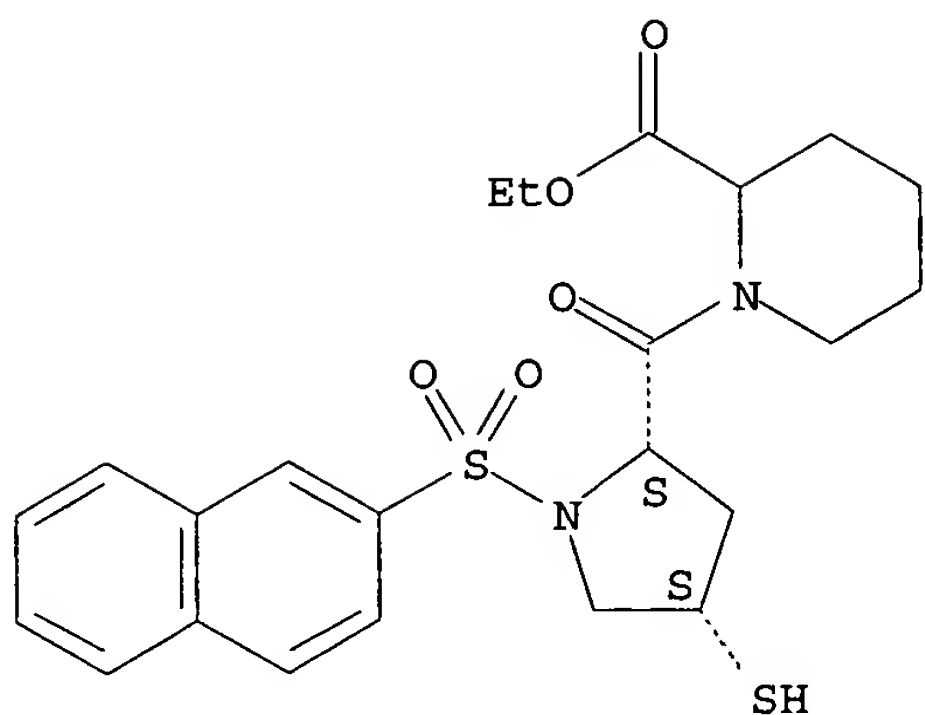
Absolute stereochemistry.



RN 393157-14-7 HCAPLUS

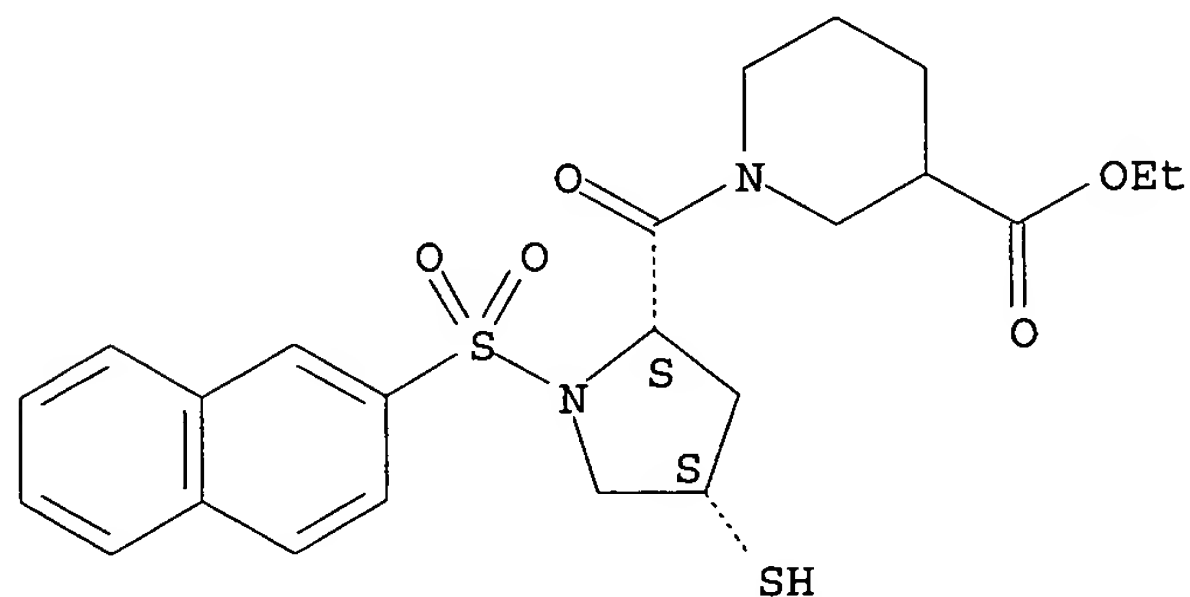
CN 2-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



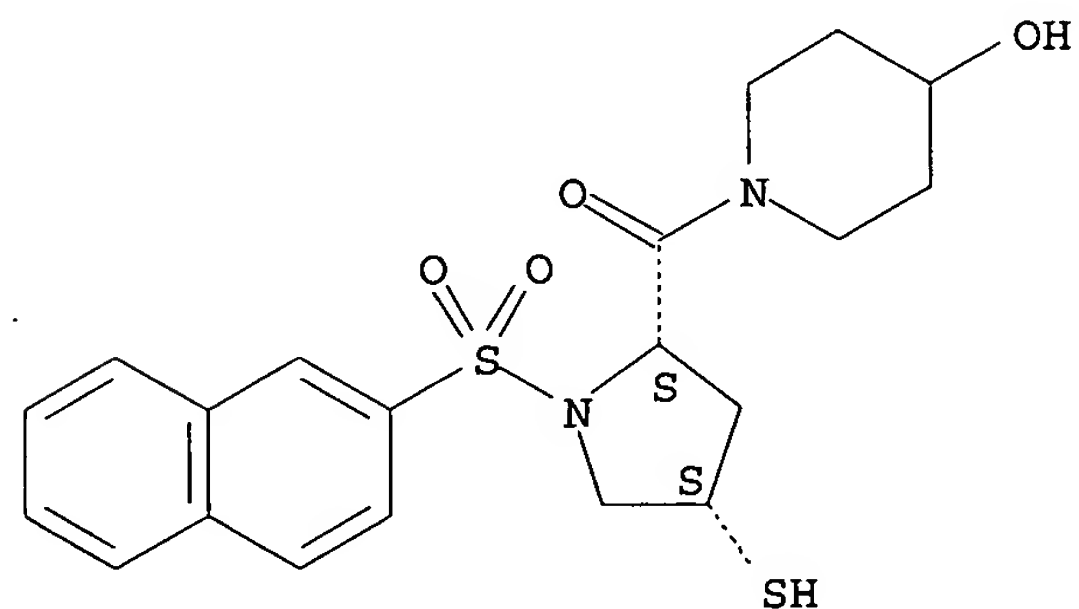
RN 393157-15-8 HCAPLUS  
 CN 3-Piperidinecarboxylic acid, 1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393157-17-0 HCAPLUS  
 CN 4-Piperidinol, 1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]- (9CI) (CA INDEX NAME)

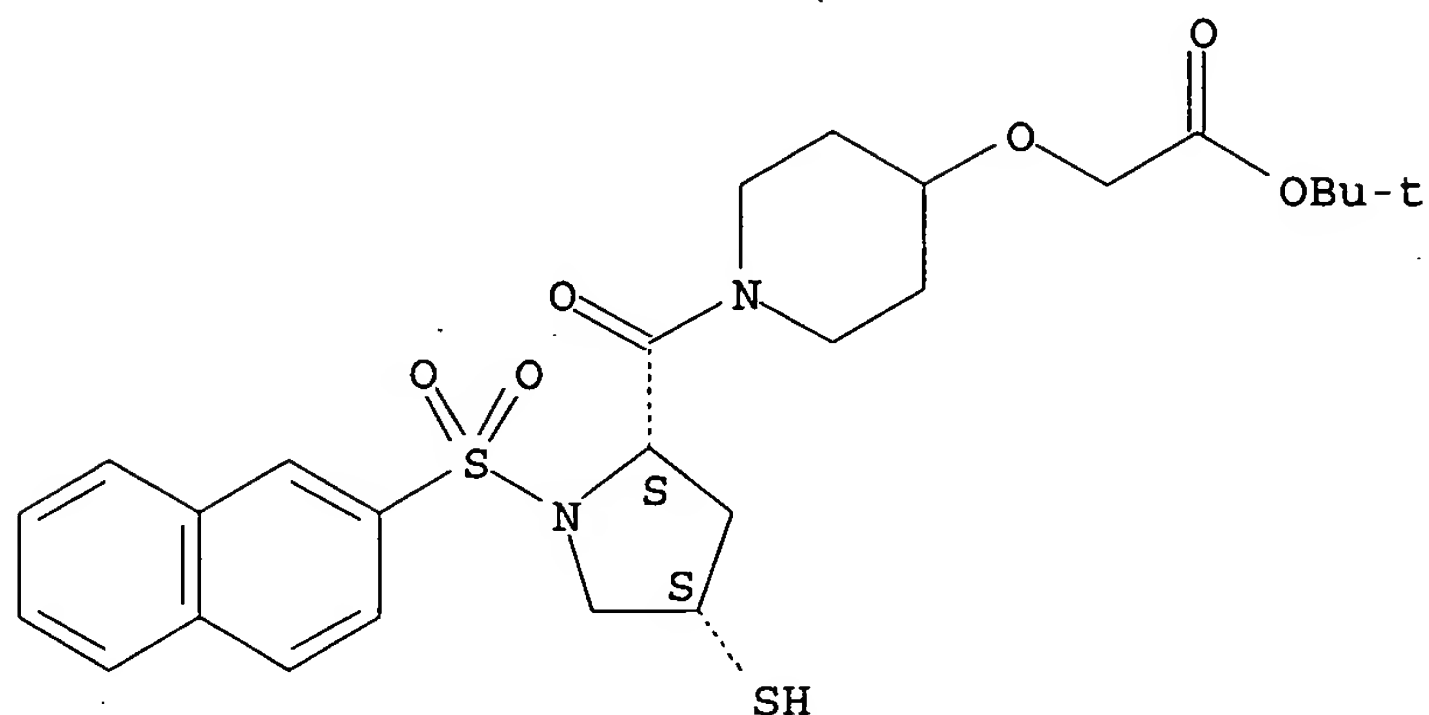
Absolute stereochemistry.



RN 393157-18-1 HCAPLUS  
 CN Acetic acid, [[1-[[[(2S,4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-2-pyrrolidinyl]carbonyl]-4-piperidinol]- (9CI)

pyrrolidinyllcarbonyl]-4-piperidinyloxy]-, 1,1-dimethylethyl ester (9CI)  
(CA INDEX NAME)

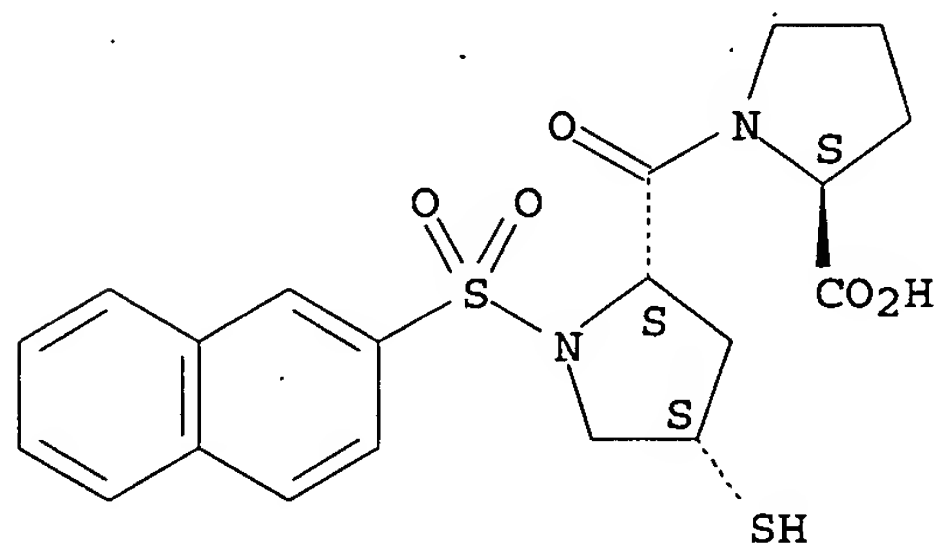
Absolute stereochemistry.



RN 393157-23-8 HCAPLUS

CN L-Proline, (4S)-4-mercapto-1-(2-naphthalenylsulfonyl)-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 391671-83-3P 391671-85-5P 391671-90-2P  
391671-92-4P 391672-17-6P 391672-19-8P  
391672-22-3P 393153-80-5P 393153-82-7P  
393153-83-8P 393153-84-9P 393153-92-9P  
393153-93-0P 393153-99-6P 393154-04-6P  
393154-69-3P 393154-78-4P 393156-49-5P  
393159-07-4P 393159-08-5P

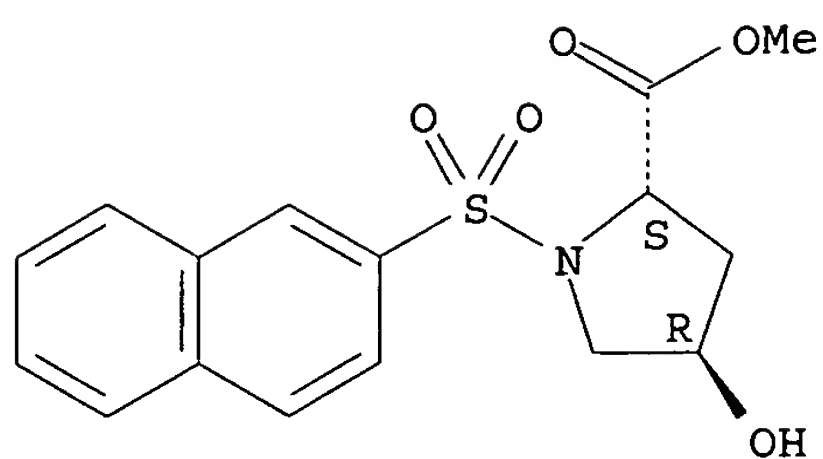
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of mercaptopyrrolidinecarboxamides as **inhibitors** of endothelin-converting **enzyme**)

RN 391671-83-3 HCAPLUS

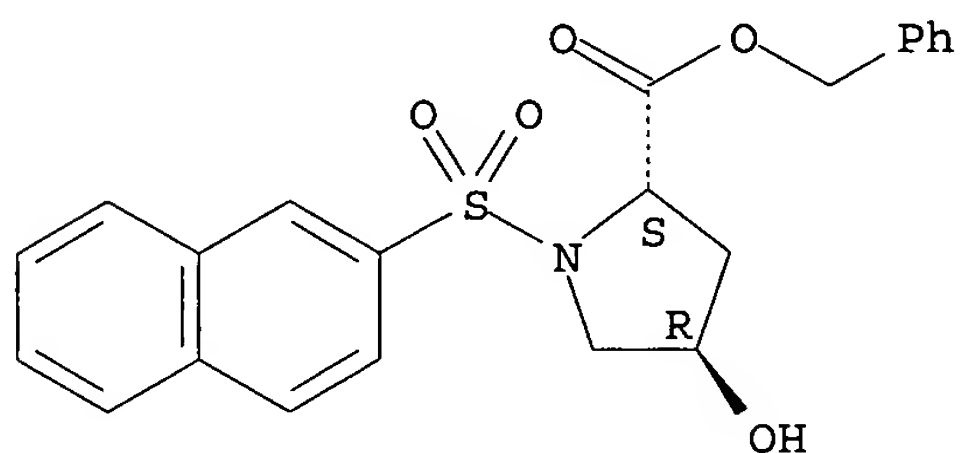
CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



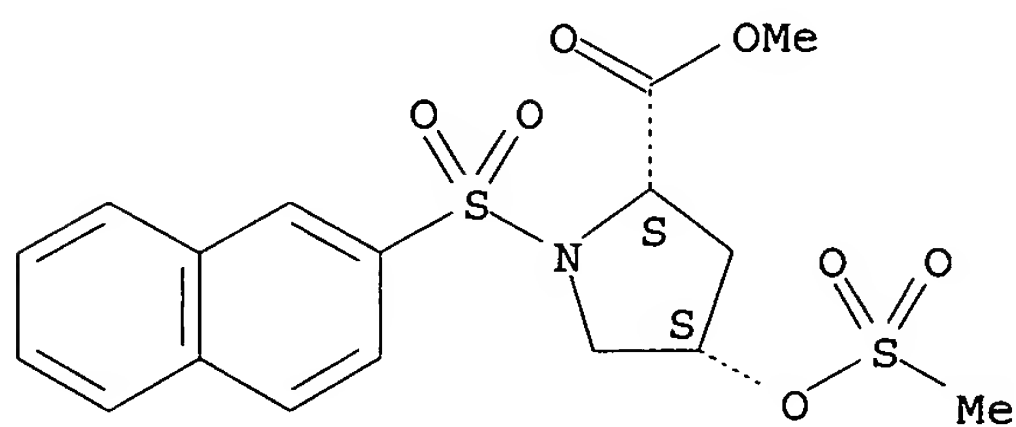
RN 391671-85-5 HCAPLUS  
 CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester,  
 (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 391671-90-2 HCAPLUS  
 CN L-Proline, 4-[(methylsulfonyl)oxy]-1-(2-naphthalenylsulfonyl)-, methyl  
 ester, (4S)- (9CI) (CA INDEX NAME)

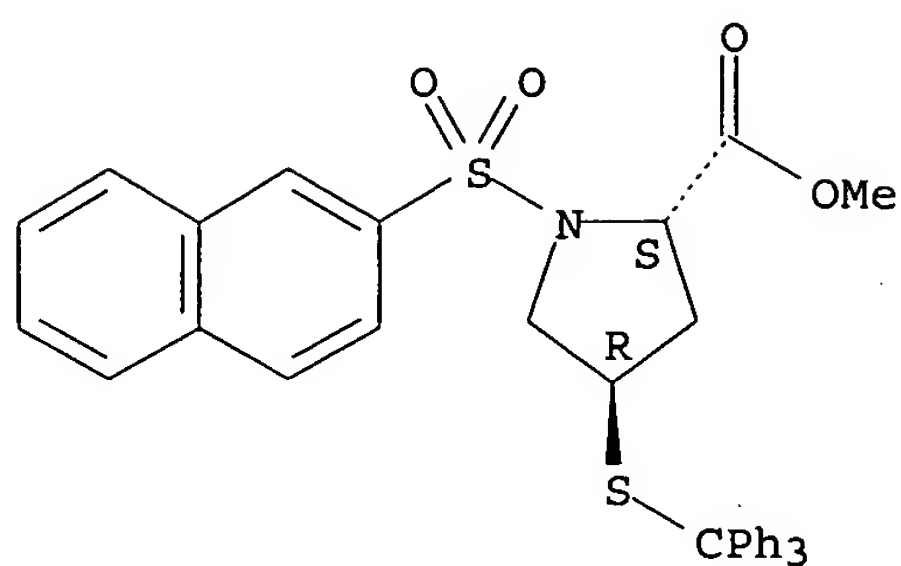
Absolute stereochemistry.



RN 391671-92-4 HCAPLUS  
 CN L-Proline, 1-(2-naphthalenylsulfonyl)-4-[(triphenylmethyl)thio]-, methyl  
 ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

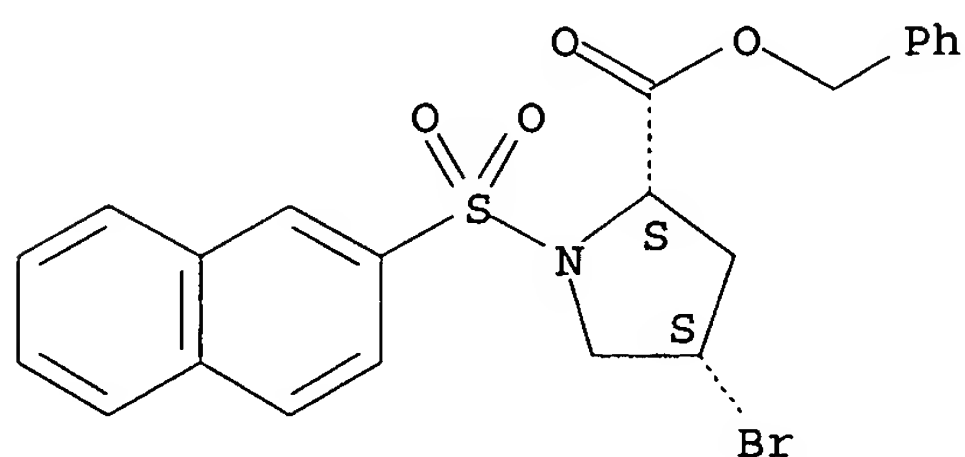




RN 391672-17-6 HCAPLUS

CN L-Proline, 4-bromo-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4S)-(9CI) (CA INDEX NAME)

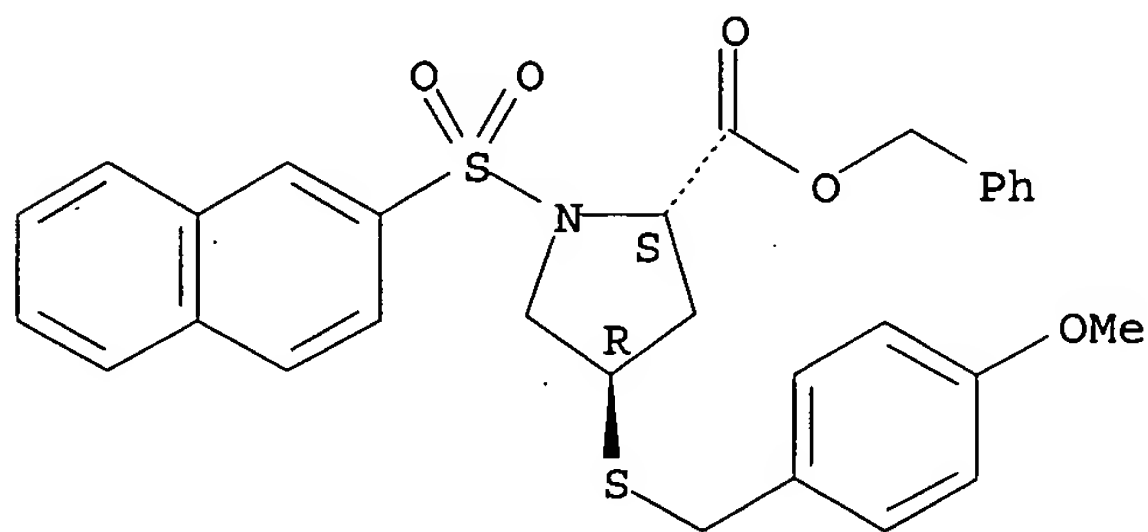
Absolute stereochemistry.



RN 391672-19-8 HCAPLUS

CN L-Proline, 4-[[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, phenylmethyl ester, (4R)-(9CI) (CA INDEX NAME)

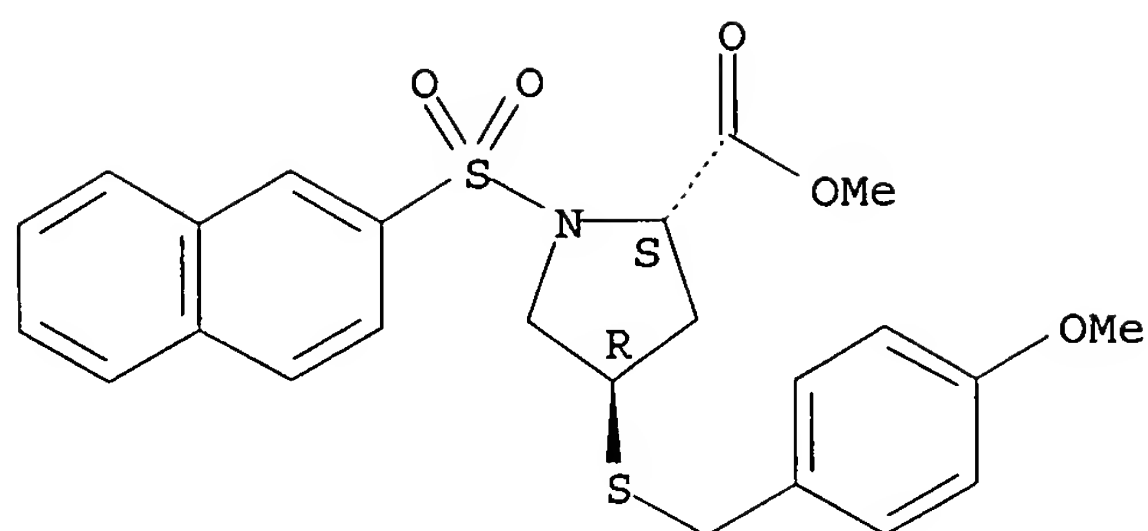
Absolute stereochemistry.



RN 391672-22-3 HCAPLUS

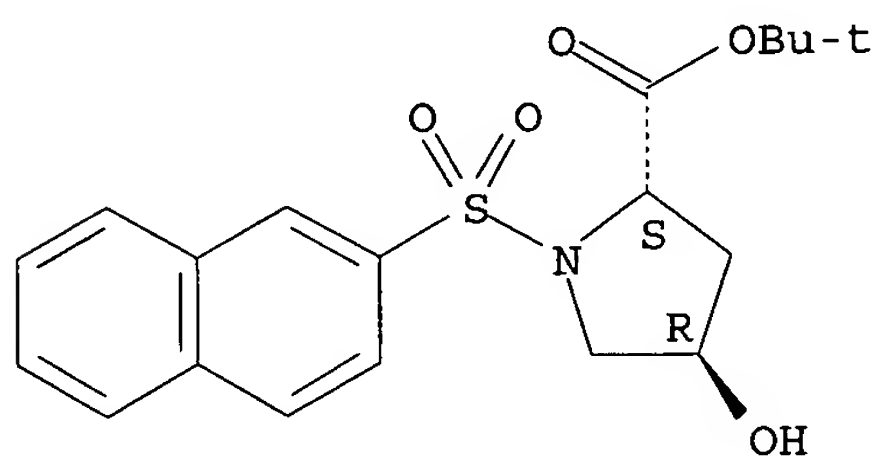
CN L-Proline, 4-[[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



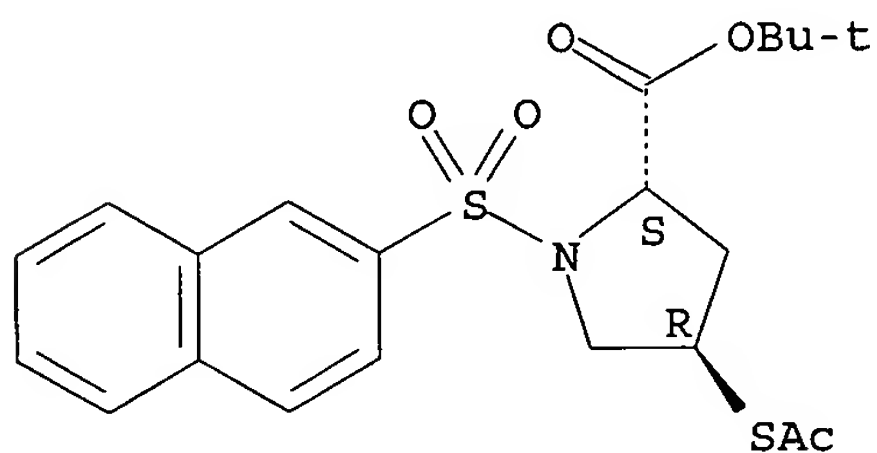
RN 393153-80-5 HCAPLUS  
 CN L-Proline, 4-hydroxy-1-(2-naphthalenylsulfonyl)-, 1,1-dimethylethyl ester,  
 (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



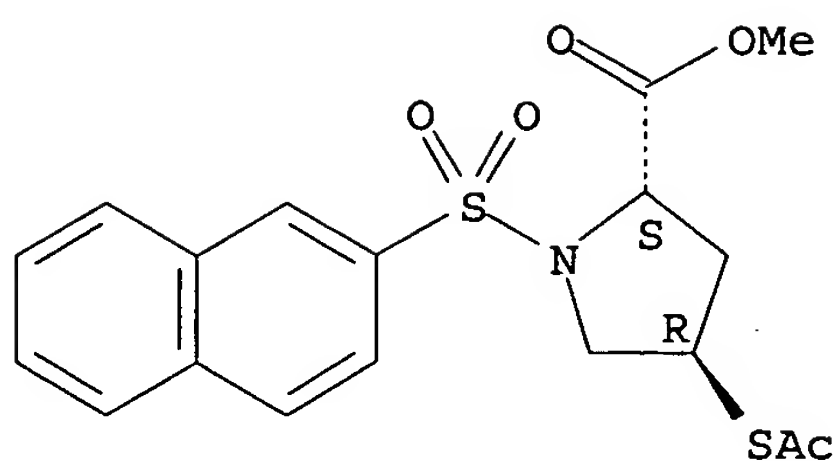
RN 393153-82-7 HCAPLUS  
 CN L-Proline, 4-(acetylthio)-1-(2-naphthalenylsulfonyl)-, 1,1-dimethylethyl  
 ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393153-83-8 HCAPLUS  
 CN L-Proline, 4-(acetylthio)-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)-  
 (9CI) (CA INDEX NAME)

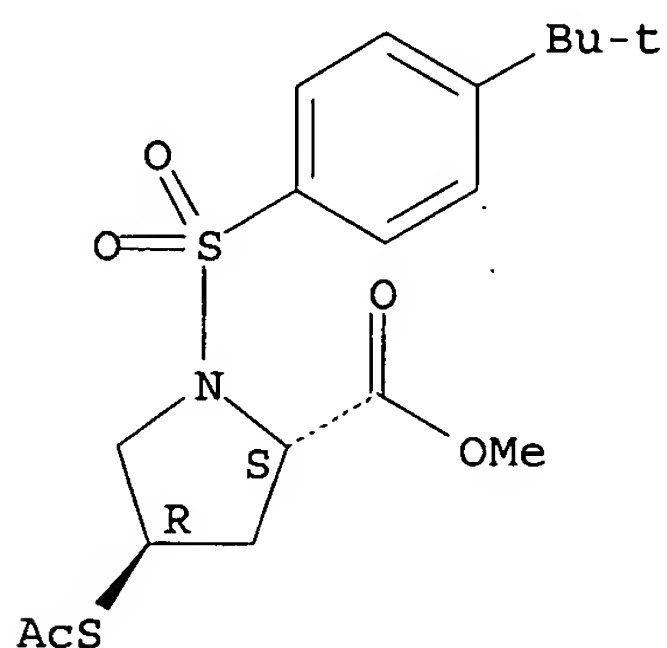
Absolute stereochemistry.



RN 393153-84-9 HCAPLUS

CN L-Proline, 4-(acetylthio)-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

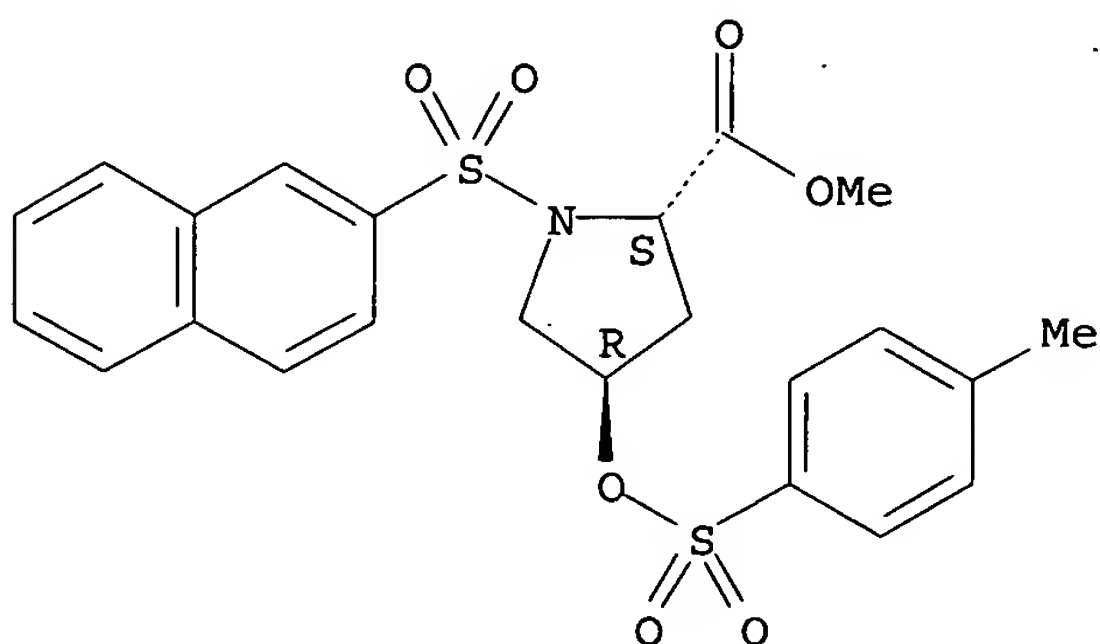
Absolute stereochemistry.



RN 393153-92-9 HCAPLUS

CN L-Proline, 4-[[4-methylphenyl]sulfonyl]oxy]-1-(2-naphthalenylsulfonyl)-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

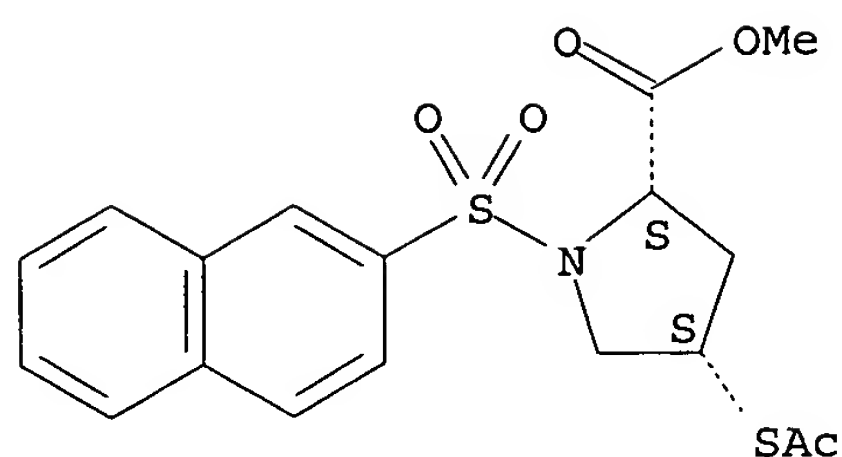
Absolute stereochemistry.



RN 393153-93-0 HCAPLUS

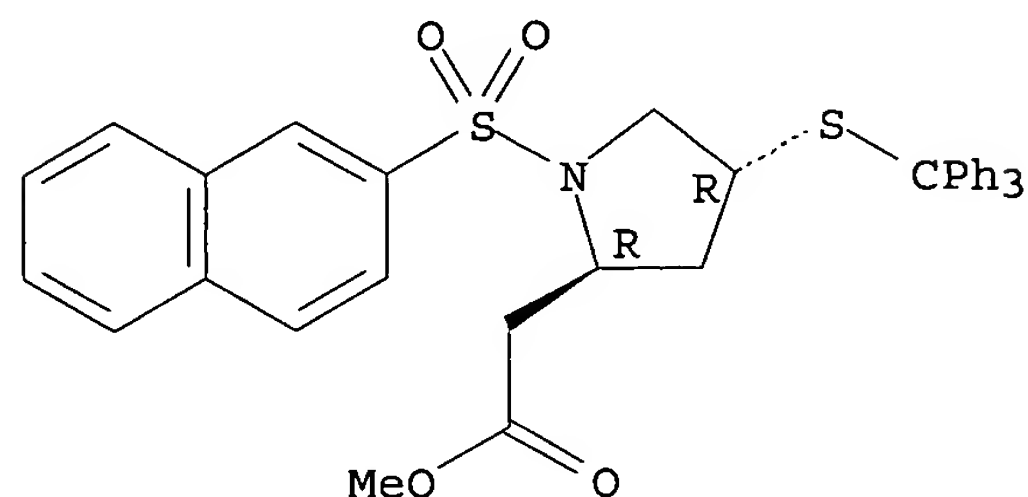
CN L-Proline, 4-(acetylthio)-1-(2-naphthalenylsulfonyl)-, methyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



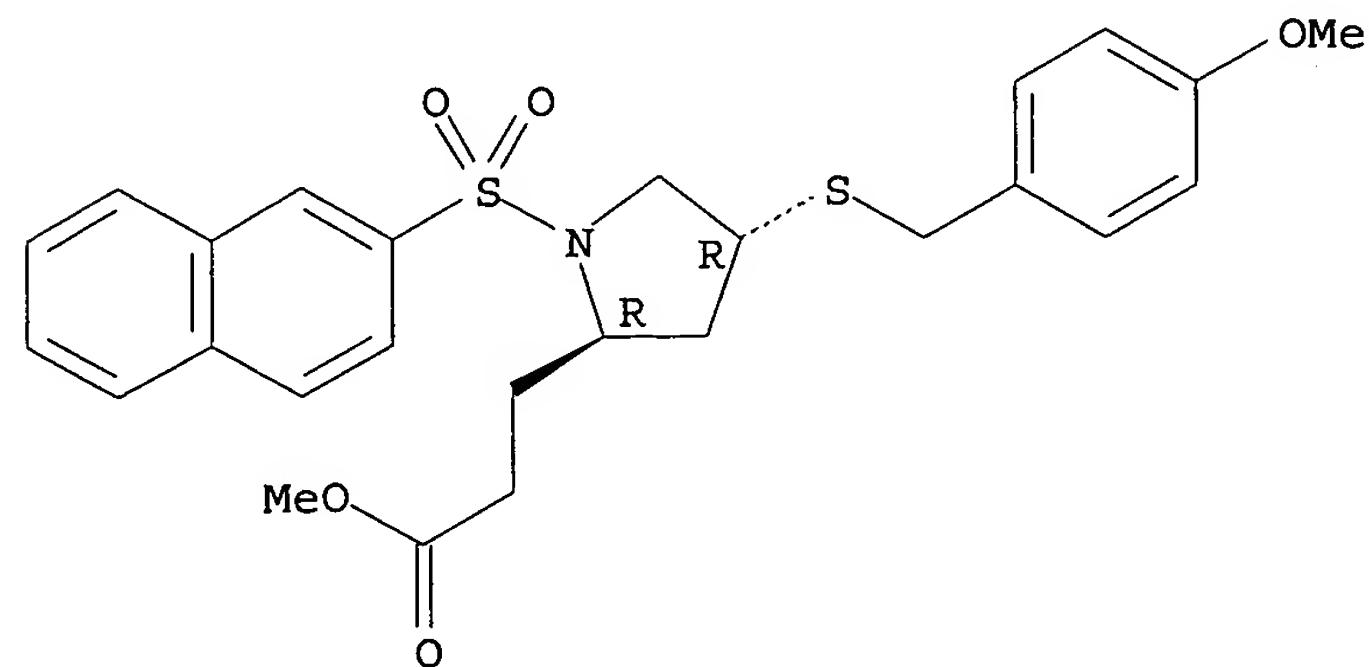
RN 393153-99-6 HCAPLUS  
 CN 2-Pyrrolidineacetic acid, 1-(2-naphthalenylsulfonyl)-4-  
 [(triphenylmethyl)thio]-, methyl ester, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



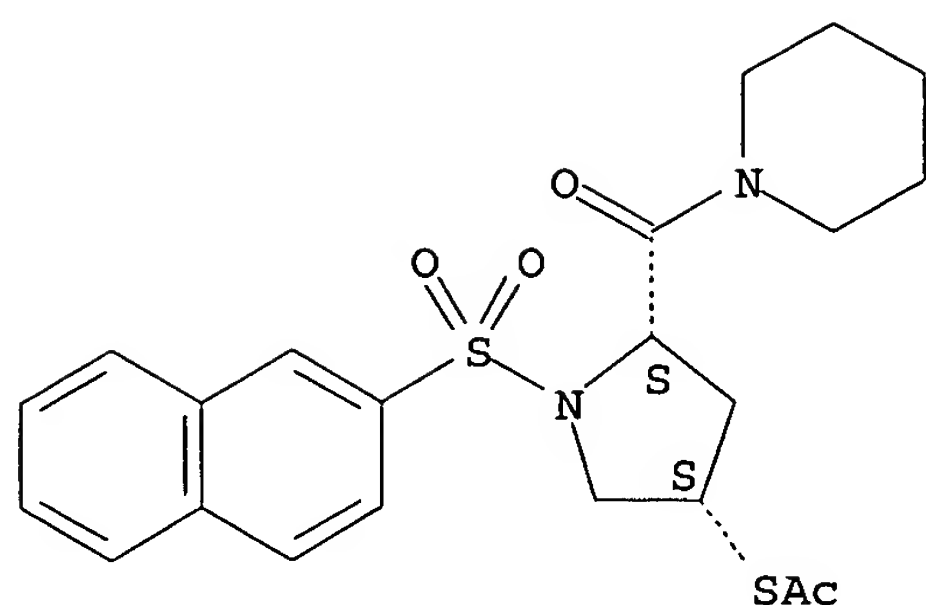
RN 393154-04-6 HCAPLUS  
 CN 2-Pyrrolidinepropanoic acid, 4-[[[4-methoxyphenyl)methyl]thio]-1-(2-  
 naphthalenylsulfonyl)-, methyl ester, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



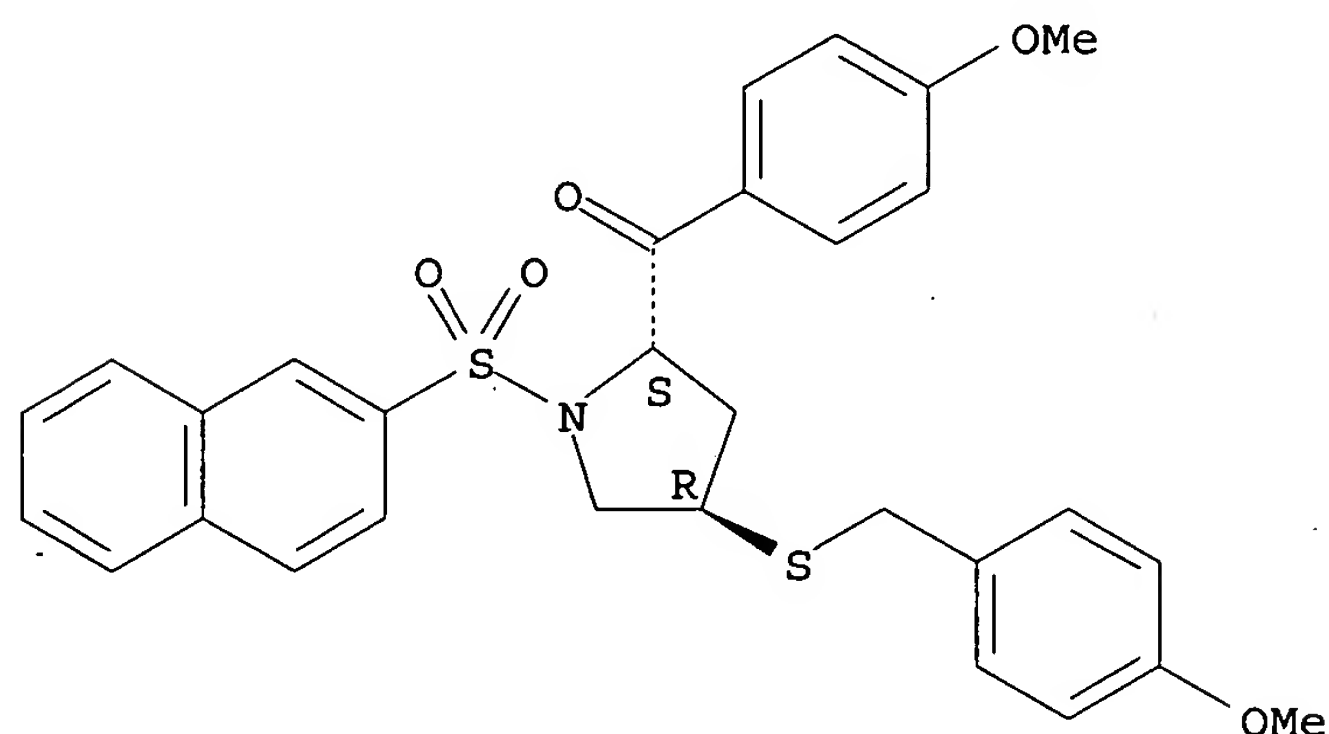
RN 393154-69-3 HCAPLUS  
 CN Ethanethioic acid, S-[(3S,5S)-1-(2-naphthalenylsulfonyl)-5-(1-  
 piperidinylcarbonyl)-3-pyrrolidinyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393154-78-4 HCAPLUS  
 CN Pyrrolidine, 2-(4-methoxybenzoyl)-4-[[[(4-methoxyphenyl)methyl]thio]-1-(2-naphthalenylsulfonyl)-, (2S,4R)- (9CI) (CA INDEX NAME)

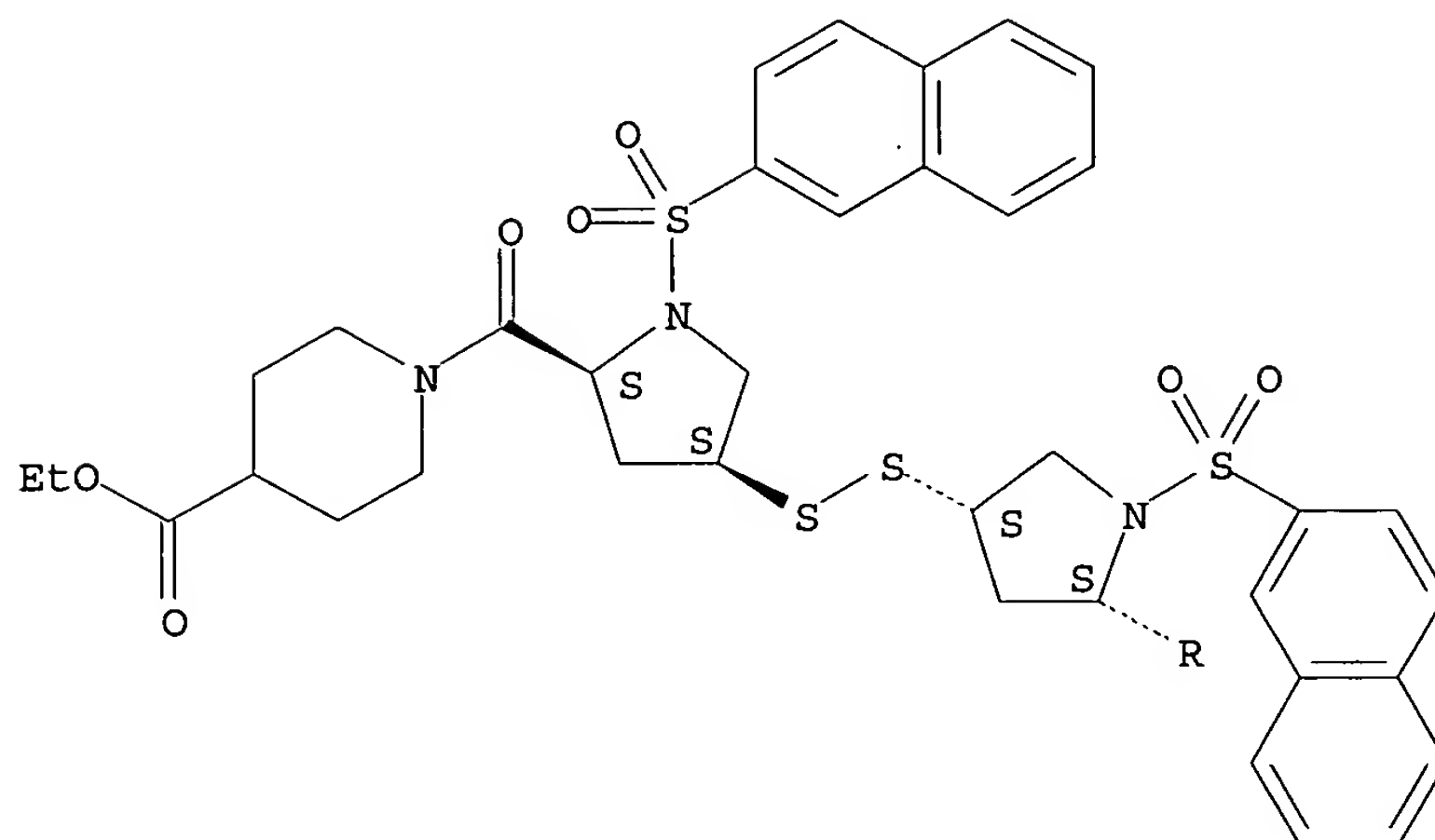
Absolute stereochemistry.



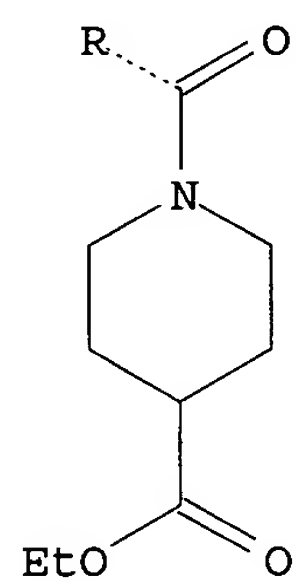
RN 393156-49-5 HCAPLUS  
 CN 4-Piperidinecarboxylic acid, 1,1'-[dithiobis[[[(2S,4S)-1-(2-naphthalenylsulfonyl)-4,2-pyrrolidinediyl]carbonyl]]bis-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

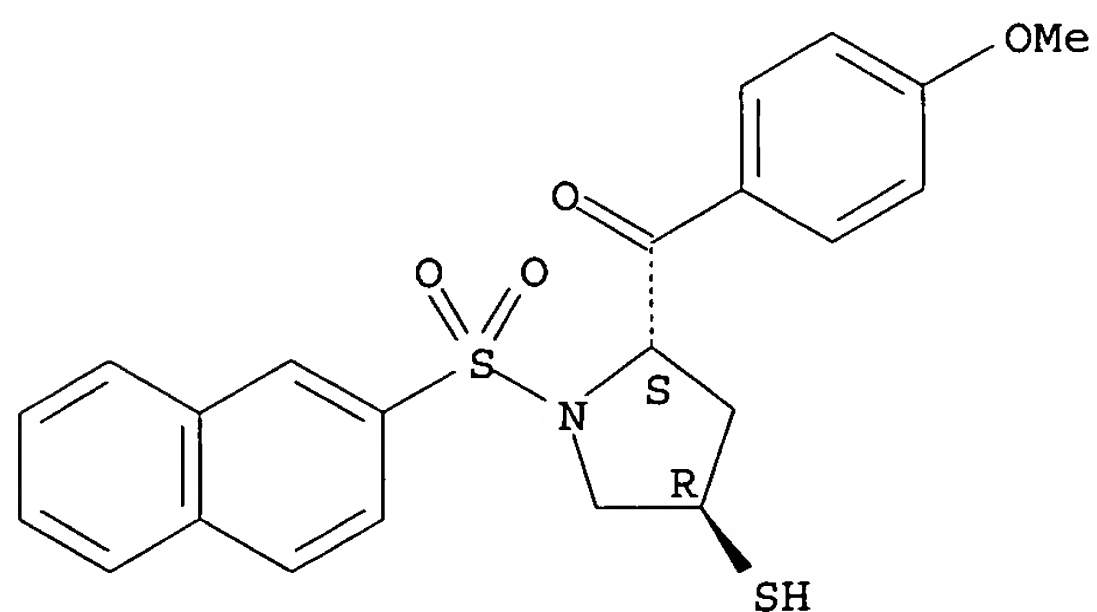


PAGE 2-A



RN 393159-07-4 HCAPLUS  
 CN 3-Pyrrolidinethiol, 5-(4-methoxybenzoyl)-1-(2-naphthalenylsulfonyl)-,  
 (3R,5S)- (9CI) (CA INDEX NAME)

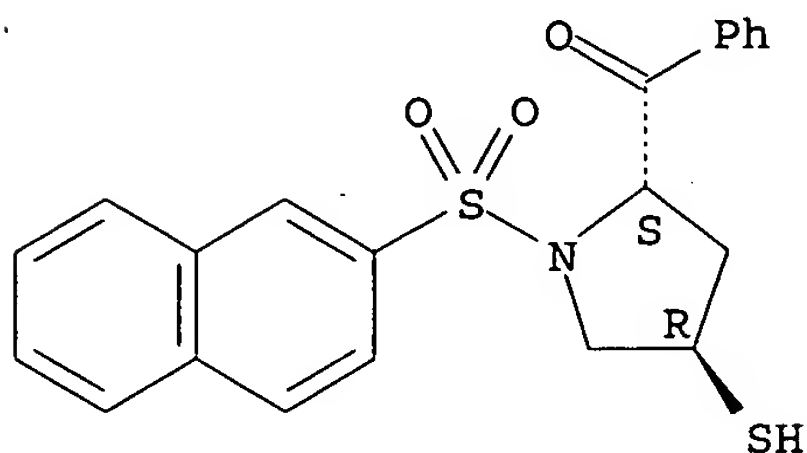
Absolute stereochemistry.



RN 393159-08-5 HCAPLUS

CN 3-Pyrrolidinethiol, 5-benzoyl-1-(2-naphthalenylsulfonyl)-, (3R,5S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:6377 HCAPLUS

DOCUMENT NUMBER: 136:69695

TITLE: Preparation of  $\beta$ -lactam compounds as inhibitors of tryptase

INVENTOR(S): Bisacchi, Gregory S.; Slusarchyk, William A.; Treuner, Uwe; Sutton, James C.; Zahler, Robert; Seiler, Steven; Kronenthal, David R.; Randazzo, Michael E.; Schwinden, Mark D.; Xu, Zhongmin; Shi, Zhongping

PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA

SOURCE: U.S., 171 pp., Cont.-in-part of U. S. Ser. No. 336,253, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

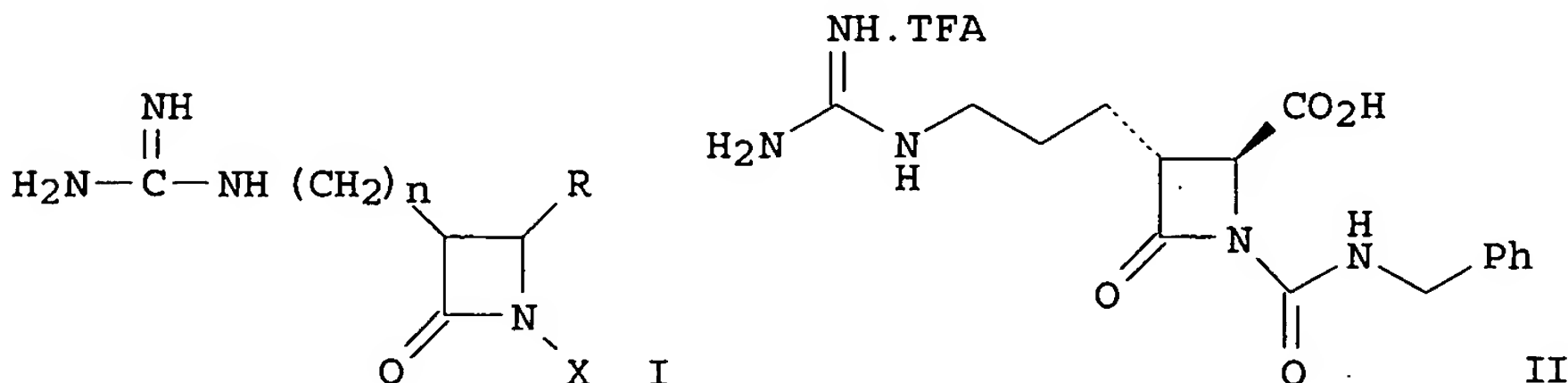
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6335324	B1	20020101	US 1999-458847	19991213 <--
PRIORITY APPLN. INFO.:			US 1998-90636P	P 19980625
			US 1999-336253	B2 19990618

OTHER SOURCE(S): MARPAT 136:69695  
GI



AB Novel  $\beta$ -lactam compds., e.g. of formula I [R = CO<sub>2</sub>H, alkoxycarbonyl, acyl, CO-heterocyclyl, etc.; X = acyl, CO-heterocyclyl, SO<sub>2</sub>-alkyl, aminoalkylphenyl, etc.; n = 1-6], are prepared These compds.

inhibit tryptase as well as other **enzyme** systems or are selective tryptase **inhibitors** and are useful as antiinflammatory agents particularly in the treatment of chronic asthma (no data). Thus, II was prepared from (4S)-N-(tert-butyldimethylsilyl)azetidin-2-one-4-carboxylic acid, 1-chloro-3-iodopropane, N,N'-bis(benzyloxycarbonyl)-1-guanylpurazole and benzyl isocyanate.

IT 253174-33-3P 253174-35-5P 253174-36-6P

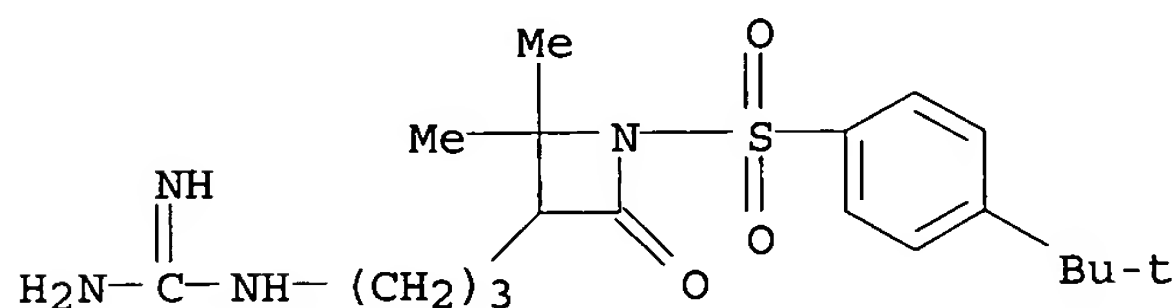
253174-39-9P 253174-40-2P 253174-53-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of  $\beta$ -lactam compds. as **inhibitors** of tryptase)

RN 253174-33-3 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4,4-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

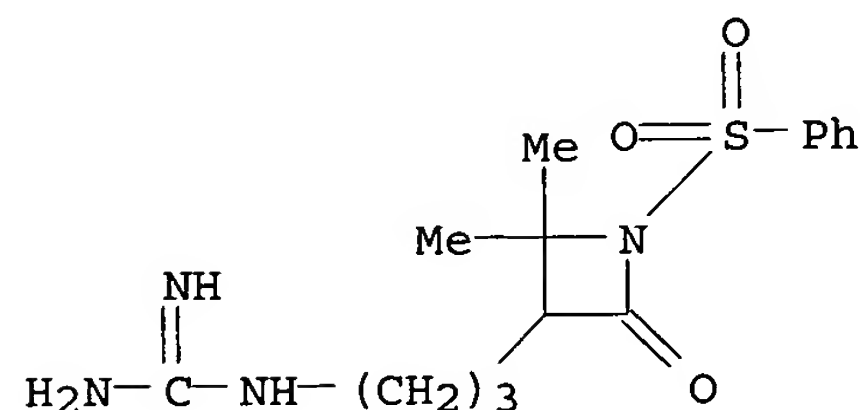
RN 253174-35-5 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 253174-34-4

CMF C15 H22 N4 O3 S

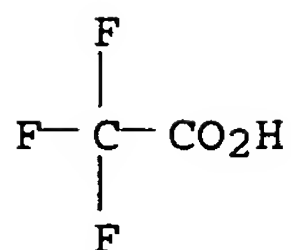


CM 2

CRN 76-05-1

CMF C2 H F3 O2

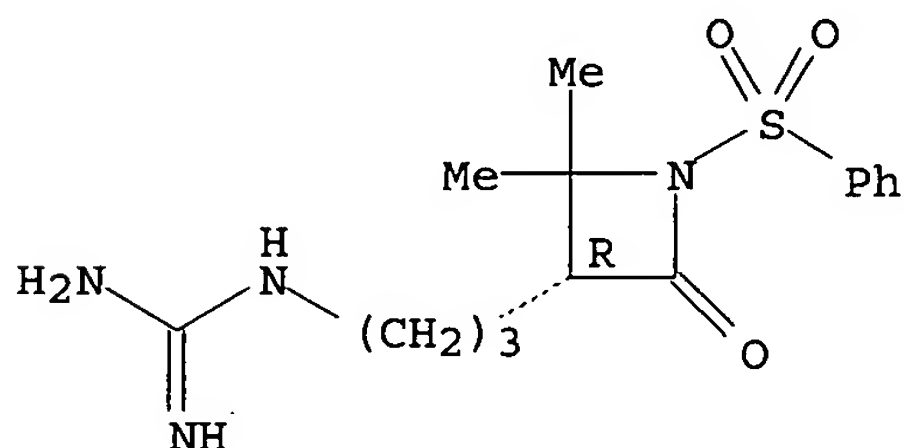




RN 253174-36-6 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

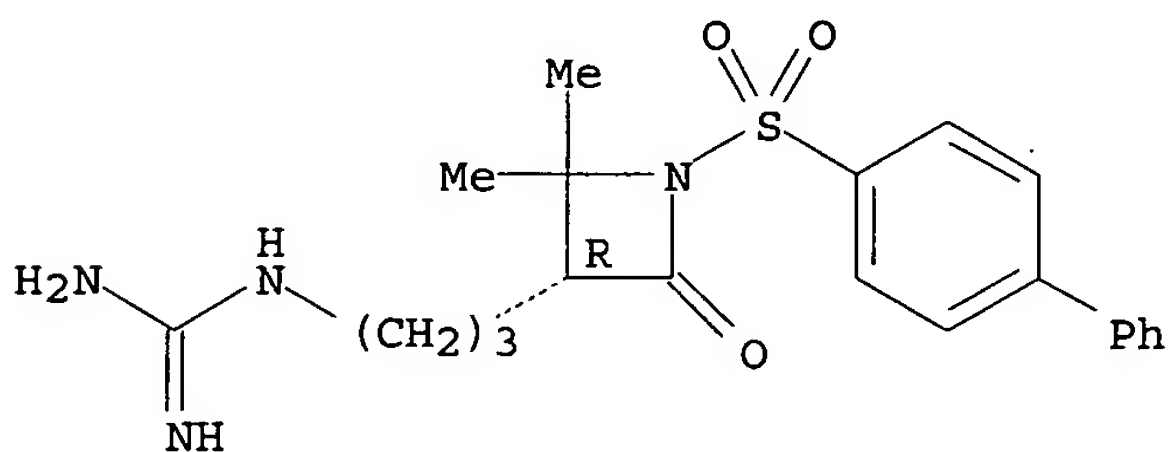


● HCl

RN 253174-39-9 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-1-([1,1'-biphenyl]-4-ylsulfonyl)-4,4-dimethyl-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

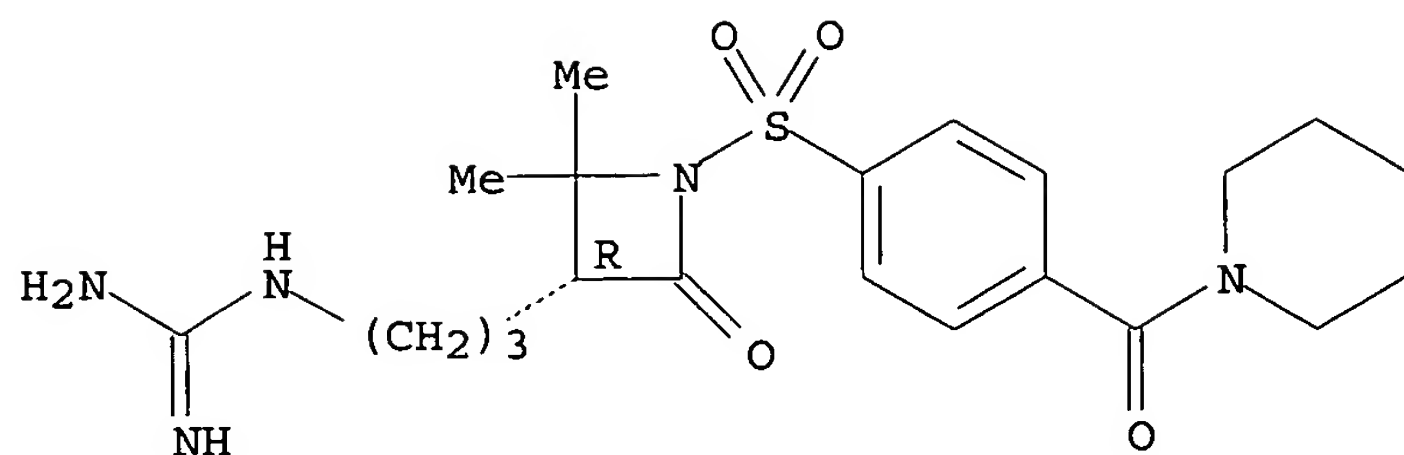


● HCl

RN 253174-40-2 HCAPLUS

CN Piperidine, 1-[4-[[[(3R)-3-[3-[(aminoiminomethyl)amino]propyl]-2,2-dimethyl-4-oxo-1-azetidinyl]sulfonyl]benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



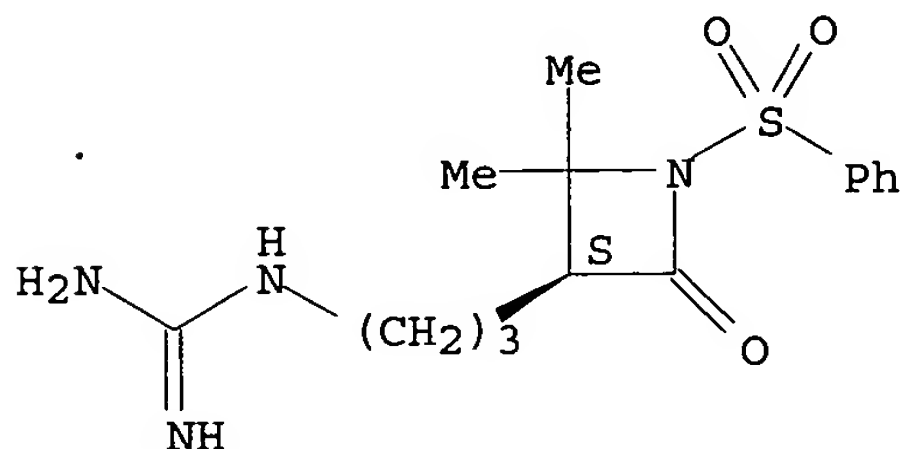
● HCl

RN 253174-53-7 HCAPLUS  
 CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)aminopropyl]-4,4-dimethyl-1-(phenylsulfonyl)-, (3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

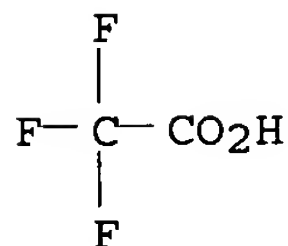
CRN 253174-52-6  
 CMF C15 H22 N4 O3 S

Absolute stereochemistry. Rotation (-).



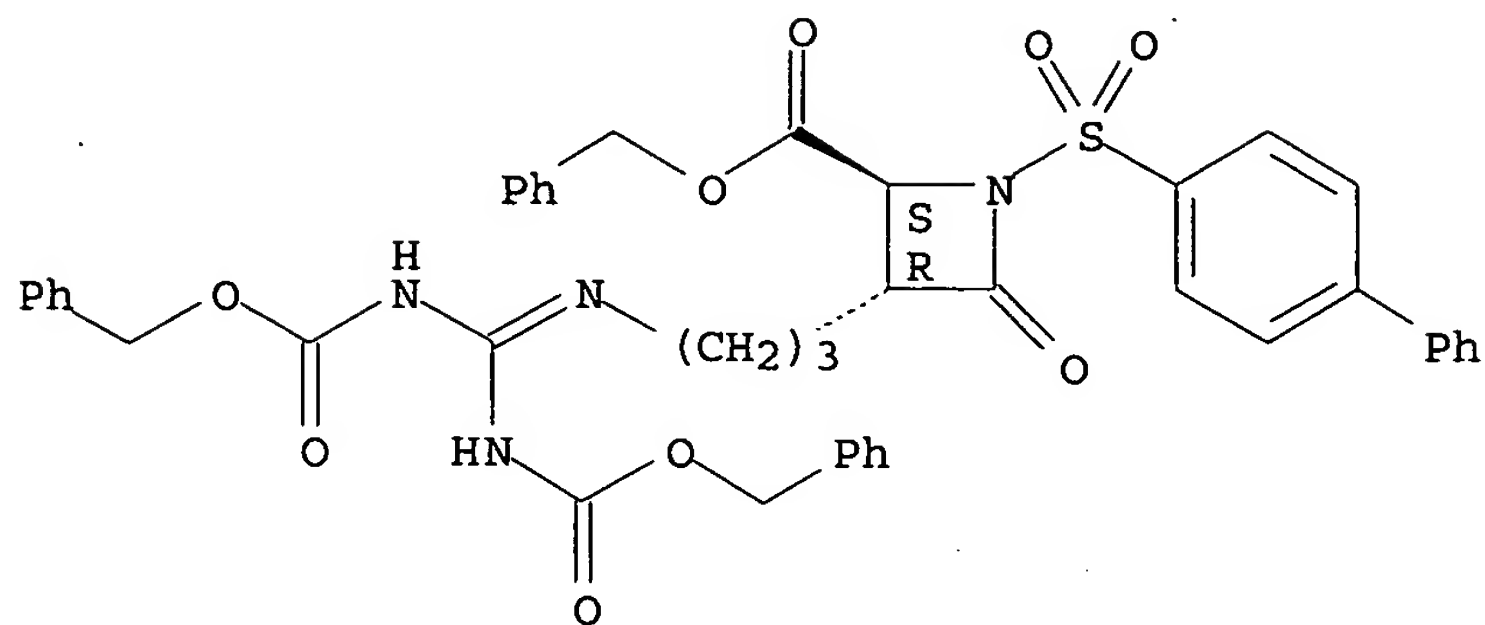
CM 2

CRN 76-05-1  
 CMF C2 H F3 O2



IT 253176-09-9P 253176-75-9P 253176-76-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of  $\beta$ -lactam compds. as inhibitors of tryptase)  
 RN 253176-09-9 HCAPLUS  
 CN 2-Azetidinecarboxylic acid, 1-([1,1'-biphenyl]-4-ylsulfonyl)-3-[3-[[bis[(phenylmethoxy)carbonyl]amino]methylene]amino]propyl]-4-oxo-, phenylmethyl ester, (2S,3R)- (9CI) (CA INDEX NAME)

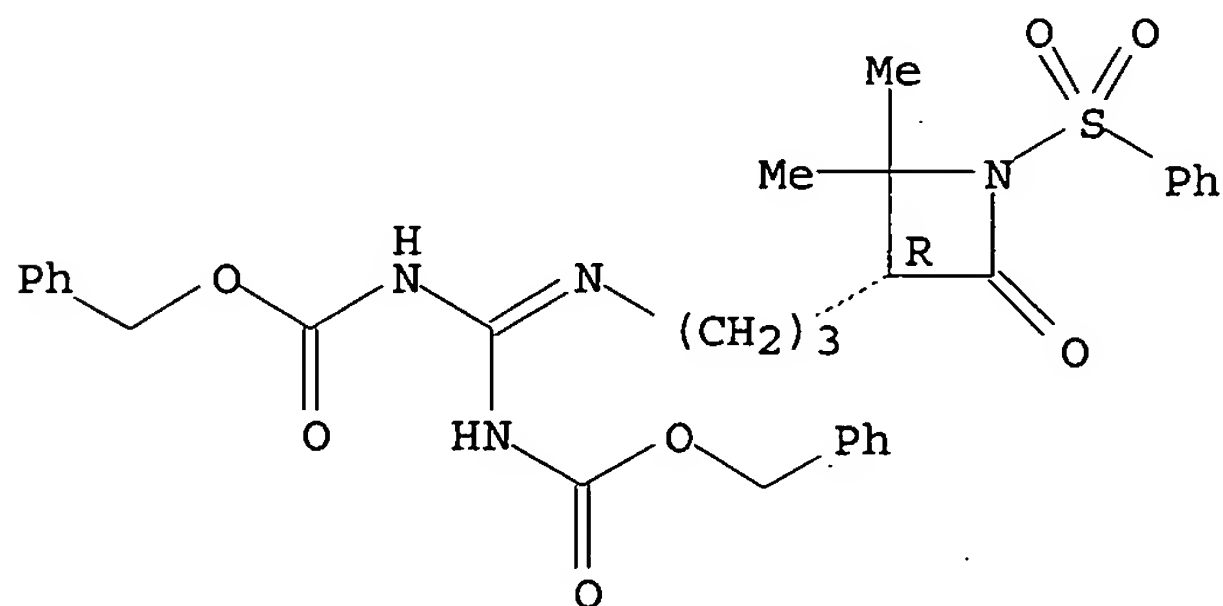
Absolute stereochemistry.



RN 253176-75-9 HCAPLUS

CN Carbamic acid, [[3-[(3R)-2,2-dimethyl-4-oxo-1-(phenylsulfonyl)-3-azetidinyl]propyl]carbonimidoyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

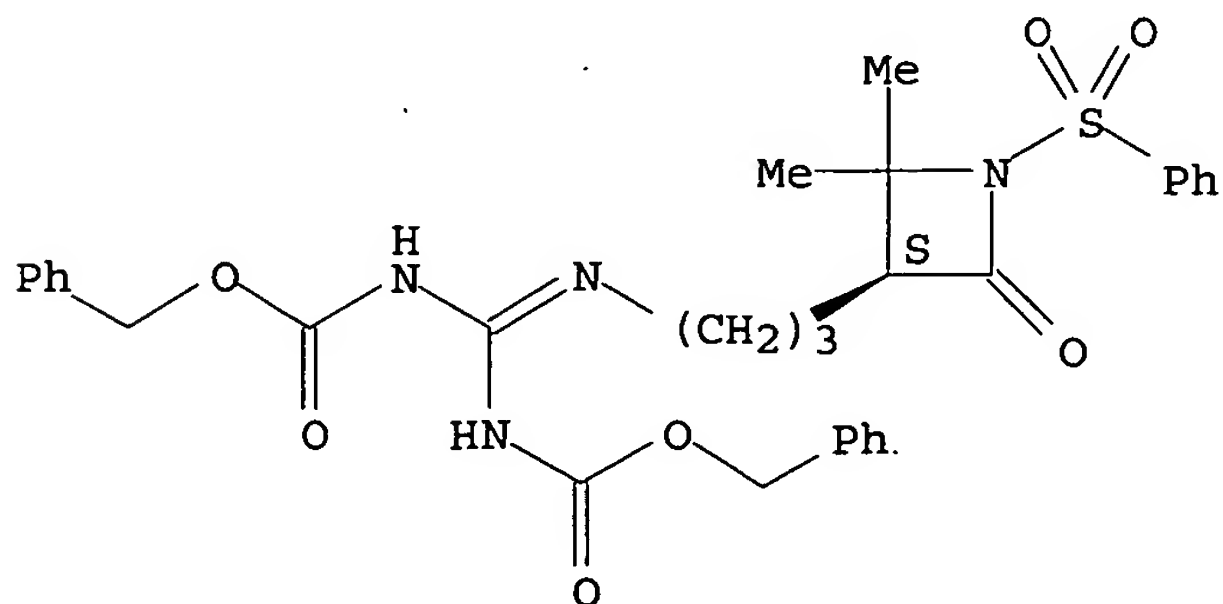
Absolute stereochemistry.



RN 253176-76-0 HCAPLUS

CN Carbamic acid, [[3-[(3S)-2,2-dimethyl-4-oxo-1-(phenylsulfonyl)-3-azetidinyl]propyl]carbonimidoyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

26

THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:762982 HCAPLUS

DOCUMENT NUMBER: 135:318704

TITLE: Preparation of benzimidazole-, benzoxazole- and  
benzothiazolesulfonamide amino acid derivatives as  
selective matrix metalloproteinase inhibitors

INVENTOR(S): Park, Young-Jun; Bae, Hae-Young; Yoo, Ji-Uk; Chae,  
Myeong-Yun; Paek, Sang-Hyun; Min, Hye-Kyung; Park,  
Hyun-Gyu; Ryu, Choon-Ho; Kim, Kyung-Chul; Lee,  
Jeoung-Wook

PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea

SOURCE: PCT Int. Appl., 115 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

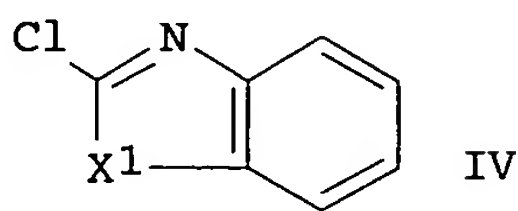
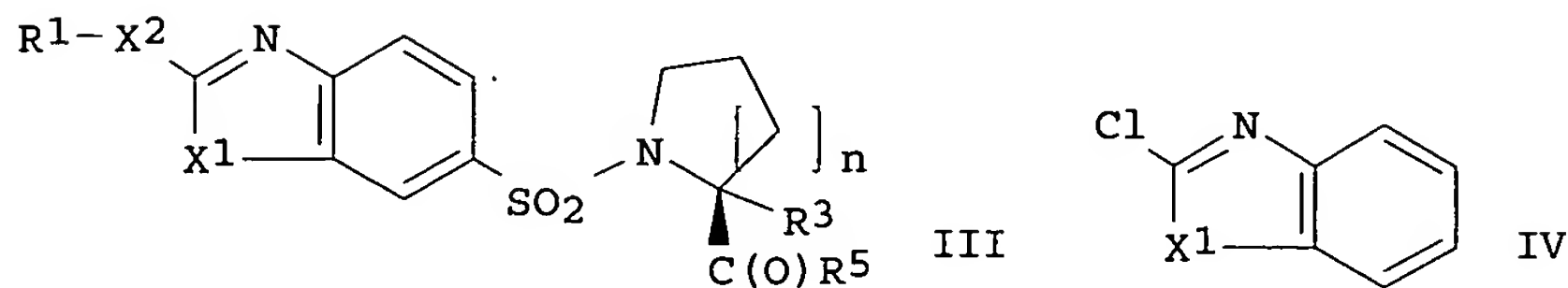
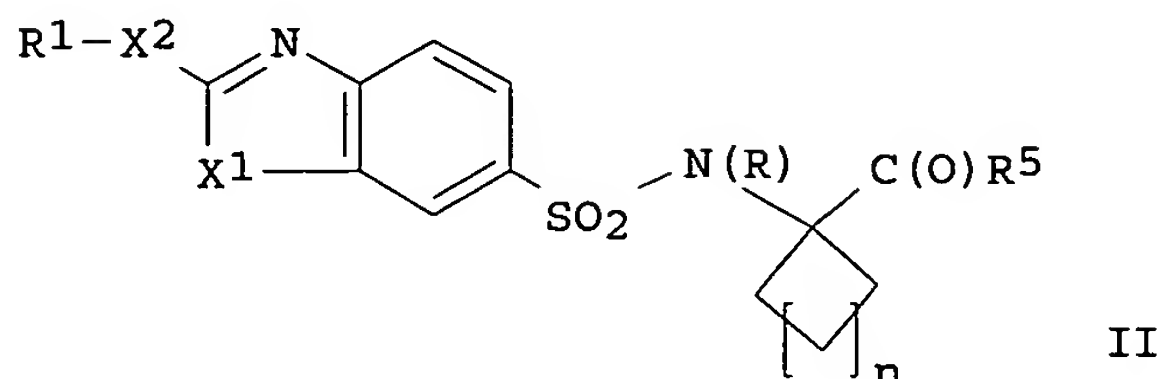
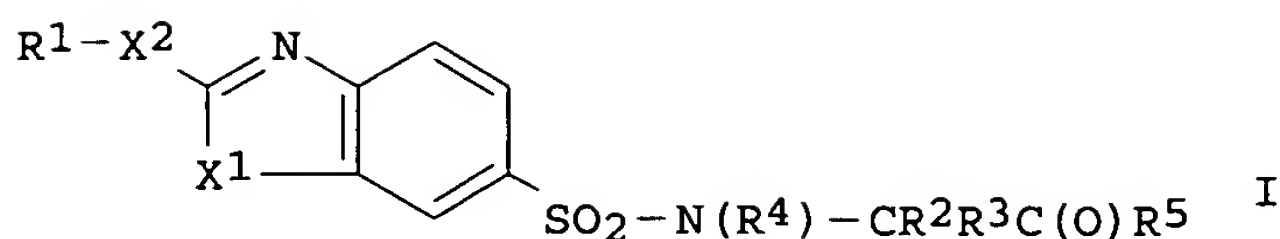
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077092	A1	20011018	WO 2001-KR585	20010407 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
KR 2001099525	A	20011109	KR 2000-18327	20000407 <--
KR 2001099526	A	20011109	KR 2000-18328	20000407 <--
KR 2001090922	A	20011022	KR 2000-18431	20000408 <--
CA 2372352	AA	20011018	CA 2001-2372352	20010407 <--
AU 2001048884	A5	20011023	AU 2001-48884	20010407 <--
EP 1208092	A1	20020529	EP 2001-922101	20010407 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003530389	T2	20031014	JP 2001-575566	20010407 <--
US 2002169314	A1	20021114	US 2001-18507	20011206 <--
US 6548667	B2	20030415		

PRIORITY APPLN. INFO.:

KR 2000-18327	A	20000407
KR 2000-18328	A	20000407
KR 2000-18431	A	20000408
WO 2001-KR585	W	20010407

OTHER SOURCE(S): MARPAT 135:318704

GI



AB The present invention provides novel sulfonamide derivs. (I (e.g. (2R)-3-methyl-2-[(2-phenylthiobenzothiazole-6-sulfonyl)amino]butanoic acid Me ester), II (n = 0-4) and III (n = 0-4)), useful as an inhibitors of matrix metalloproteinase (MMP), its isomers, pharmaceutically acceptable salts thereof and a process for preparing the same. Since the sulfonamide derivs. of the present invention selectively inhibit MMP activity in vitro, the MMP inhibitors comprising the sulfonamide derivs. as an effective ingredient can be practically applied for the prevention and treatment of all sorts of diseases caused by overexpression and overactivation of MMP. In I: R1 denotes H, C1-12 alkyl, carbocyclic aryl-lower alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl-lower alkyl, (oxo, amino or thio) C3-7 cycloalkyl, (oxo, amino or thio) C3-7 cycloalkyl-lower alkyl, C2-12 lower alkenyl, C2-12 lower alkynyl, carbocyclic aryl, heterocyclic aryl, heterocyclic aryl-lower alkyl, biaryl, halo lower alkyl, biaryl-lower alkylarylalkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, alkyl or aryl (thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, acylamino lower alkyl, (N-lower alkylpiperazino, or N-carbocyclic or heterocyclic aryl-lower alkylpiperazino)-lower alkyl or (morpholino, thiomorpholino, piperidino, pyrrolidino or piperidyl)-lower alkyl. R2 denotes H, lower alkyl, carbocyclic aryl-lower alkyl, C1-4 carbocyclic aryl-lower alkyl, C1-4 heterocyclic aryl-lower alkyl, C1-5 alkoxyphenyl-lower alkyl, C1-5 alkenoxyphenyl-lower alkyl, C1-5 alkynoxyphenyl-lower alkyl, heterocyclic aryl-lower alkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, thio-lower alkyl, alkyl or aryl (thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, carboxy-lower alkyl, (amino, mono or dialkylamino) lower alkyl or acylamino lower alkyl. R3 denotes H or C1-6-lower alkyl. R4 denotes H, C1-12 alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl-lower alkyl, (oxo, amino or thio) C3-7 cycloalkyl, (oxo, amino or thio) C3-7 cycloalkyl-lower alkyl, carbocyclic aryl, carbocyclic aryl-lower alkyl, heterocyclic aryl, heterocyclic aryl-lower alkyl, biaryl, biaryl-lower alkyl, halo lower alkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, alkyl or aryl (thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, acylamino lower alkyl, carboxy lower alkyl, (N-lower alkylpiperazino, or

N-carbocyclic or heterocyclic aryl piperazino)-lower alkyl or (morpholino, thiomorpholino, piperidino, pyrrolidino or piperidyl)-lower alkyl. R5 denotes hydroxy, alkoxy, halogen, thiol, thioalkoxy or hydroxylamine. X1 and X2 denote N-R7 (R7 is H, C1-6-lower alkyl, aryl, heteroaryl or arylalkyl), S or O. I can be prepared by (i) reacting a sulfonyl halide with H<sub>2</sub>NCR<sub>2</sub>R<sub>3</sub>CO<sub>2</sub>R<sub>6</sub> (R<sub>6</sub> = protecting group) in an organic solvent in the presence of a base to give a sulfonamide; (ii) replacing the H on N using R<sub>4</sub>-L (L = reactive leaving group) in an organic solvent in the presence of a base; and (iii) hydrolyzing the intermediate to give I (R<sub>5</sub> = OH), or further condensing I (R<sub>5</sub> = OH) to prepare I (R<sub>5</sub> = NHOH). Alternatively, I can be prepared by (i) chlorosulfonylating IV; (ii) reacting this intermediate with an amino acid derivative in an organic solvent in the

presence

of base to give a sulfonamide; (iii) heating this intermediate and R<sub>1</sub>-X<sub>2</sub>H together at 70 to 80° in an organic solvent in the presence of base to cause substitution for Cl; (iv) reacting this intermediate with R<sub>4</sub>-L (L = reactive leaving group) in an organic solvent in the presence of base to cause substitution for H on N; and, (v) hydrolyzing this intermediate into I (R<sub>5</sub> = OH), or further condensing I (R<sub>5</sub> = OH) to prepare I (R<sub>5</sub> = NHOH).

.apprx.70 Example prepns. of intermediates and products are given.

Inhibition rates for some of the claimed compds. are reported for gelatinase A (MMP-2), gelatinase B (MMP-9) and collagenase (MMP-1).

IT 367517-01-9P, (2R)-N-[2-(n-Pentylthio)benzothiazole-6-sulfonyl]-2-methoxycarbonylpyrrolidine

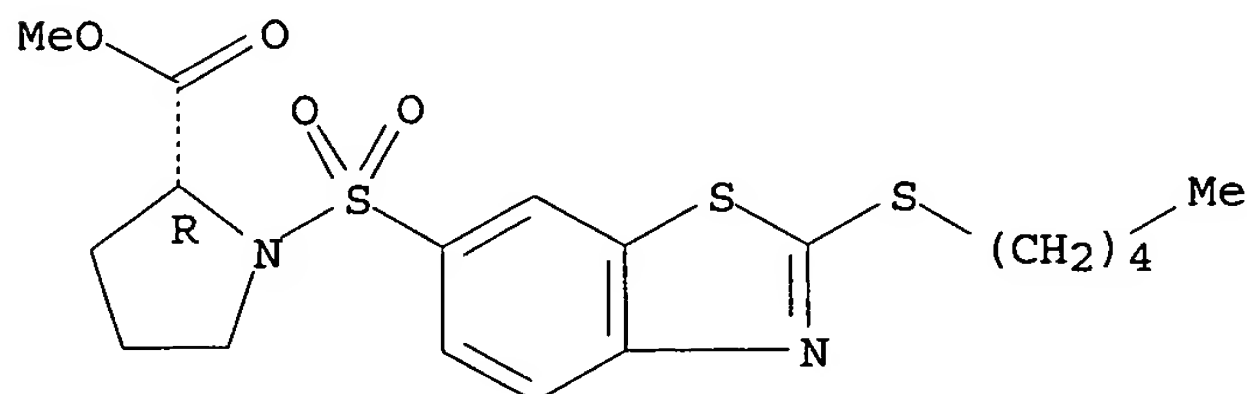
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of benzimidazole-, benzoxazole- and benzothiazolesulfonamide amino acid derivs. as selective matrix metalloproteinase inhibitors)

RN 367517-01-9 HCAPLUS

CN D-Proline, 1-[[2-(pentylthio)-6-benzothiazolyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:565008 HCAPLUS

DOCUMENT NUMBER: 135:137406

TITLE: Preparation of  $\alpha$ -sulfonyl hydroxamic acid derivatives as matrix metalloproteinase and TNF-alpha converting **enzyme inhibitors**

INVENTOR(S): Sandanayaka, Vincent Premarana; Zask, Arie; Venkatesan, Aranapakam Mudumbai; Baker, Jannie Lea; Krishnan, Lalitha; Megati, Sreenivasulu; Zeldis, Joseph

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 91 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055112	A1	20010802	WO 2001-US2669	20010125 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2398561	AA	20010802	CA 2001-2398561	20010125 <--
EP 1252143	A1	20021030	EP 2001-905121	20010125 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001007862	A	20021105	BR 2001-7862	20010125 <--
JP 2003520852	T2	20030708	JP 2001-555054	20010125 <--
PRIORITY APPLN. INFO.:			US 2000-492975	A 20000127
			WO 2001-US2669	W 20010125

OTHER SOURCE(S): MARPAT 135:137406

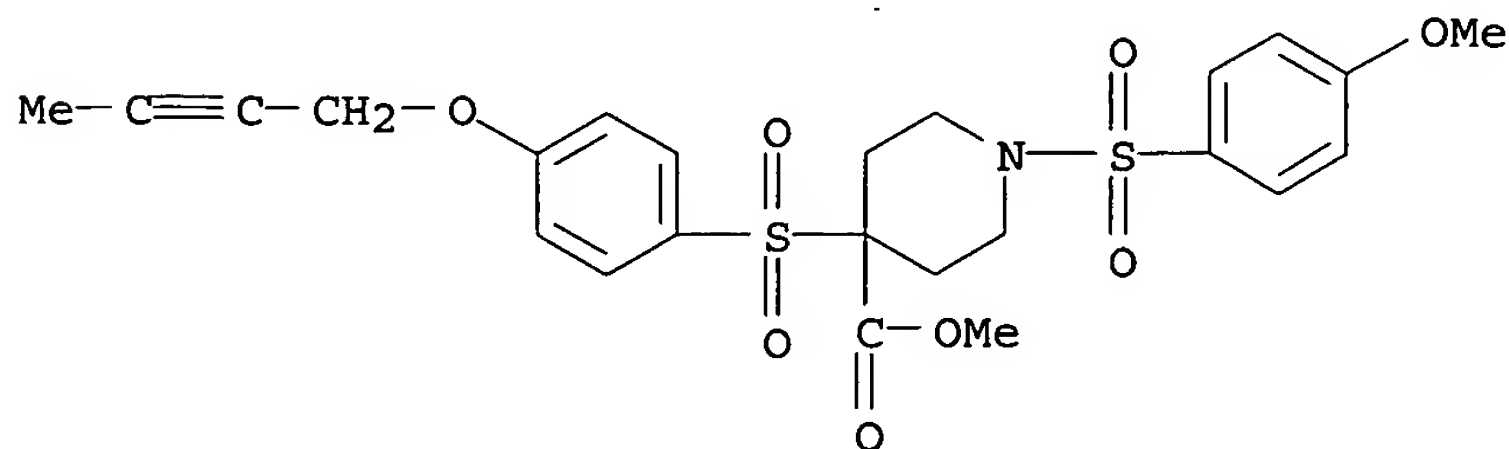
AB XONYCOCCR1R2SO2R3 [X = H, alkyl, trimethylsilyl, etc.; Y = H, alkyl, aryl, etc.; R1, R2 = H, aryl, heteroaryl, cycloalkyl, etc.; R3 = alkyl, alkenyl, alkynyl, etc.] were prepared as matrix metalloproteinase (MMP) and TNF-alpha converting enzyme (TACE) inhibitors, phosphodiesterase inhibitors, renin inhibitors, antithrombotics, and 5-lipoxygenase inhibitors (no data). E.g., a multistep synthesis of 1-benzyl-3-(4-methoxybenzenesulfonyl)piperidine-3-carboxylic acid hydroxamide is reported.

IT 287202-66-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of  $\alpha$ -sulfonyl hydroxamic acid derivs. as matrix metalloproteinase and TNF-alpha converting enzyme inhibitors)

RN 287202-66-8 HCAPLUS

CN 4-Piperidinecarboxylic acid, 4-[[4-(2-butynyloxy)phenyl]sulfonyl]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:314178 HCAPLUS

DOCUMENT NUMBER: 134:326767

TITLE: Preparation of acetylenic  $\alpha$ -amino acid-based  
sulfonamide hydroxamic acid TACE inhibitorsINVENTOR(S): Levin, Jeremy I.; Chen, James M.; Cole, Derek C.; Du,  
Mila T.; Laakso, Leif M.

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: U.S., 109 pp.  
CODEN: USXXAMDOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6225311	B1	20010501	US 2000-492691	20000127 <--
US 2003008849	A1	20030109	US 2000-748912	20001227 <--
US 2003212049	A1	20031113	US 2003-376871	20030227 <--
US 6716833	B2	20040406		
US 2004033988	A1	20040219	US 2003-377008	20030227
US 6812227	B2	20041102		
PRIORITY APPLN. INFO.:			US 1999-155249P	P 19990127
			US 2000-492691	A3 20000127
			US 2000-748912	B1 20001227

OTHER SOURCE(S): MARPAT 134:326767

AB Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO<sub>2</sub>, P(O)R<sub>10</sub>, where R<sub>10</sub> = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH<sub>2</sub>, S; R<sub>1</sub> = H, aryl, alkyl, alkenyl, alkynyl; R<sub>2</sub> = any group given for R<sub>1</sub>, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R<sub>1</sub> and R<sub>2</sub> may form a ring; R<sub>3</sub> = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R<sub>1</sub> and R<sub>3</sub> may form a ring; R<sub>4</sub>, R<sub>5</sub> = H, alkyl, CN, C.tplbond.CH; R<sub>6</sub> = any group given for R<sub>1</sub>, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepared as **inhibitors** of TNF- $\alpha$  converting **enzyme** (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-methylbutyramide was prepared and showed IC<sub>50</sub> = 7.4 nM for **inhibition** of TACE.

IT 287408-00-8P

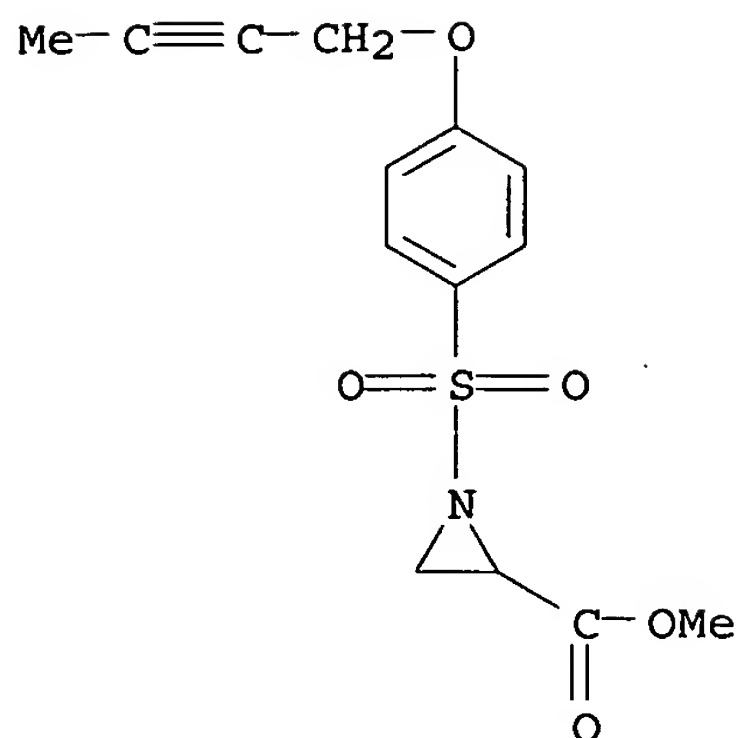
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of acetylenic  $\alpha$ -amino acid-based sulfonamide hydroxamic acid TACE **inhibitors**)

RN 287408-00-8 HCAPLUS

CN 2-Aziridinecarboxylic acid, 1-[[4-(2-butynyloxy)phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:824218 HCAPLUS

DOCUMENT NUMBER: 134:4752

TITLE: Preparation of hydroxamic acid derivatives as matrix metalloprotease inhibitors

INVENTOR(S): Bedell, Louis J.; McDonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.; Getman, Daniel P.; Decrescenzo, Gary A.; Villamil, Clara I.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: PCT Int. Appl., 380 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

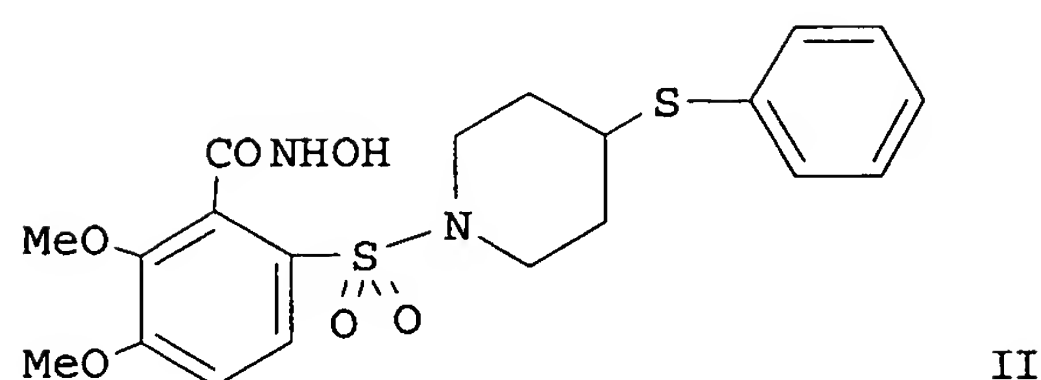
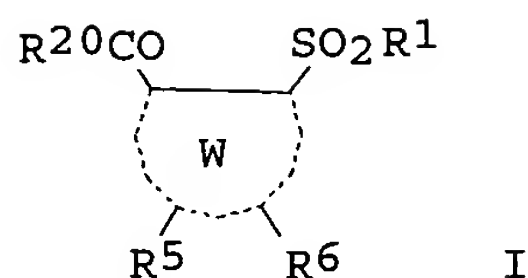
FAMILY ACC. NUM. COUNT: 10

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069819	A1	20001123	WO 2000-US6713	20000512 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2373500	AA	20001123	CA 2000-2373500	20000512 <--
EP 1177173	A1	20020206	EP 2000-931910	20000512 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000011291	A	20020514	BR 2000-11291	20000512 <--
JP 2002544257	T2	20021224	JP 2000-618236	20000512 <--
NZ 515197	A	20040326	NZ 2000-515197	20000512
ZA 2001009007	A	20030131	ZA 2001-9007	20011031 <--
PRIORITY APPLN. INFO.:			US 1999-310813	A 19990512
			WO 2000-US6713	W 20000512

OTHER SOURCE(S): MARPAT 134:4752

GI



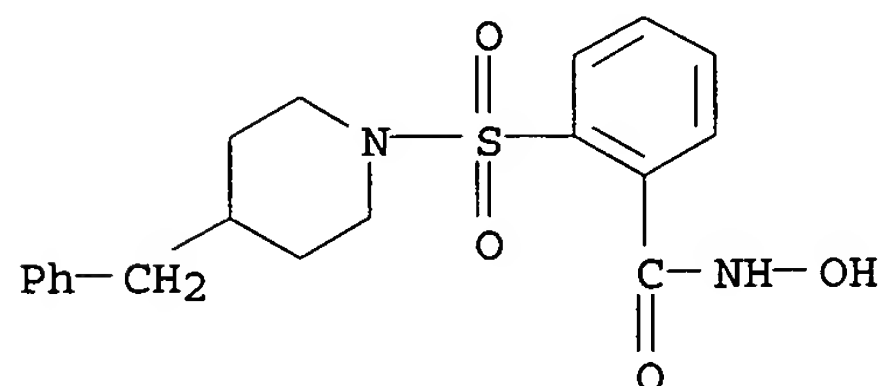
AB Title compds. [I; W = 5, 6 membered aromatic, heteroarom. ring; R = 5, 6 membered cyclohydrocarbonyl, heterocyclo, aryl, heteroaryl; R<sup>5</sup>, R<sup>6</sup> independently = hydrido, alkyl, cycloalkyl, acylalkyl, halo, nitro, hydroxyl, cyano, alkoxy, haloalkyl, haloalkyloxy, hydroxyalkyl, etc; R<sup>20</sup> = alkoxy, aryloxy, alkoxyamino, benzyloxyamino, etc] and pharmaceutically acceptable salts with inter alia **inhibits** matrix metalloprotease activity are disclosed and a treatment that comprises administering a contemplated sulfonyl aromatic or heteroarom. hydroxamic acid in an MMP **enzyme-inhibiting** effective amount to a host having a condition associated with pathol. matrix metalloprotease activity are claimed. Thus, the title compound II was prepared and MMP-2, MMP-3, MMP-8, MMP-13, and MT1-MMP **inhibition** activities were assayed.

IT 213012-59-0P 308385-44-6P 308385-45-7P  
308385-63-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of hydroxamic acid derivs. as matrix metalloprotease **inhibitors**)

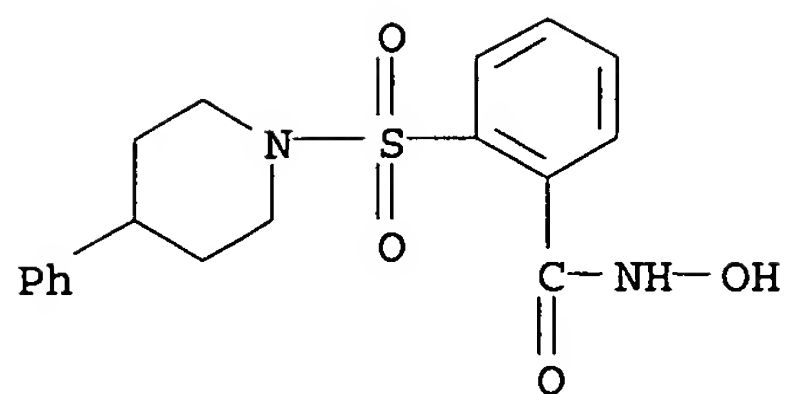
RN 213012-59-0 HCAPLUS

CN Benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl] - (9CI)  
(CA INDEX NAME)



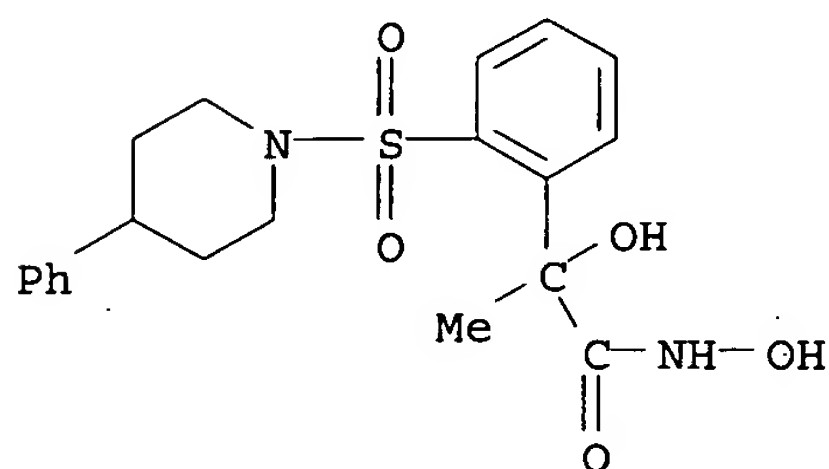
RN 308385-44-6 HCAPLUS

CN Benzamide, N-hydroxy-2-[(4-phenyl-1-piperidinyl)sulfonyl] - (9CI) (CA INDEX NAME)



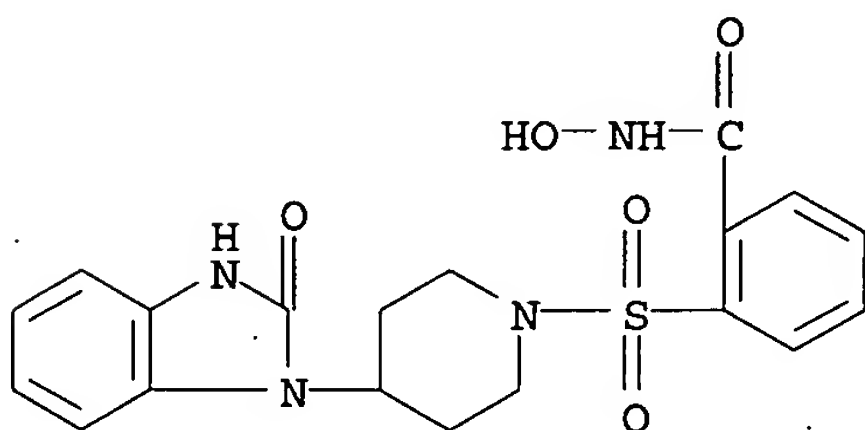
RN 308385-45-7 HCAPLUS

CN Benzeneacetamide, N,α-dihydroxy-α-methyl-2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 308385-63-9 HCAPLUS

CN Benzamide, 2-[[4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]sulfonyl]-N-hydroxy- (9CI) (CA INDEX NAME)



IT 213012-83-0P 213012-84-1P 213012-85-2P

308386-04-1P 308386-05-2P 308386-06-3P

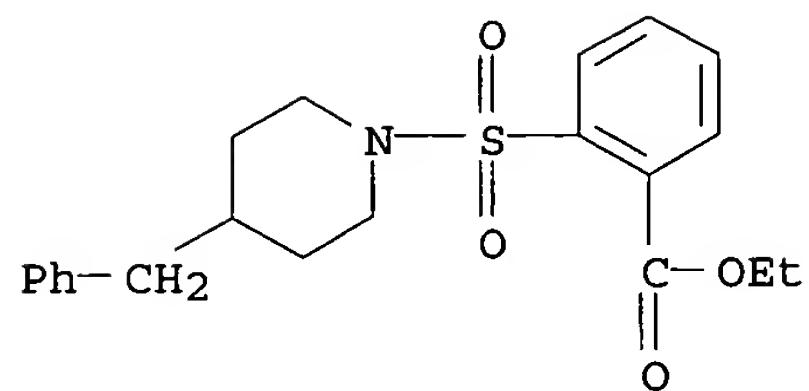
308386-07-4P 308386-08-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

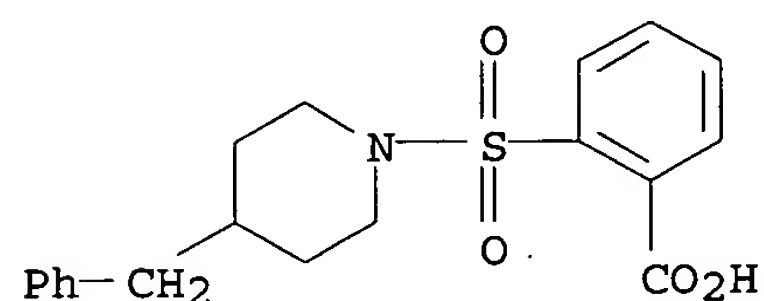
(preparation of hydroxamic acid derivs. as matrix metalloprotease inhibitors)

RN 213012-83-0 HCAPLUS

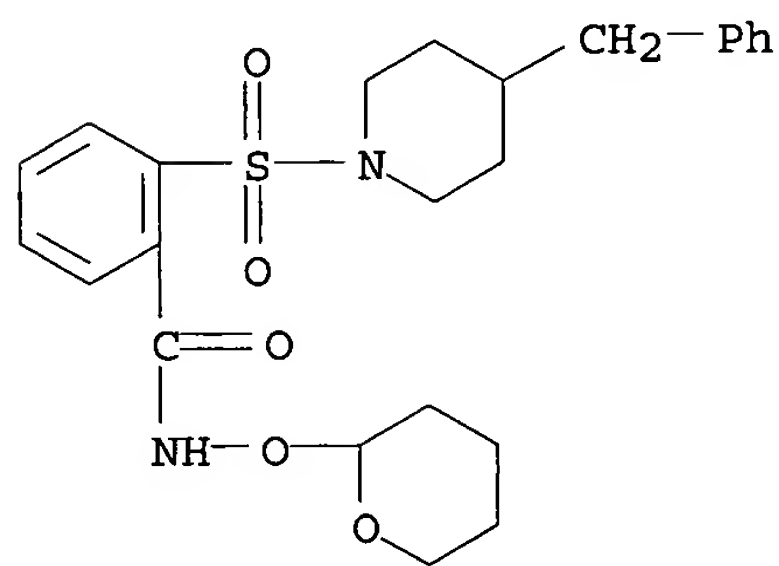
CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)



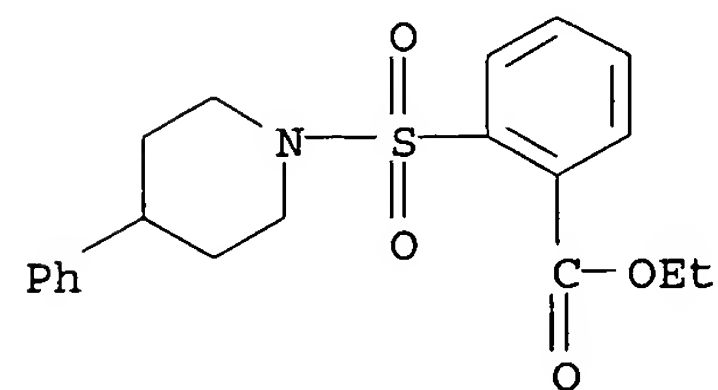
RN 213012-84-1 HCAPLUS  
 CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



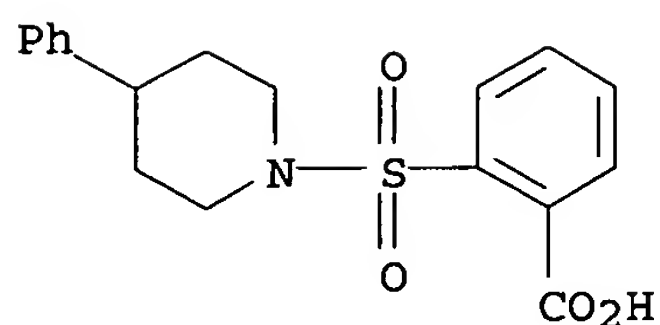
RN 213012-85-2 HCAPLUS  
 CN Benzamide, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



RN 308386-04-1 HCAPLUS  
 CN Benzoic acid, 2-[(4-phenyl-1-piperidinyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

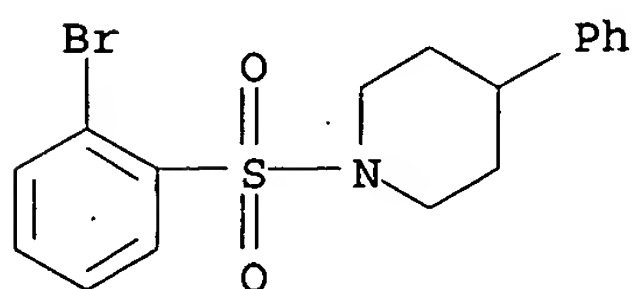


RN 308386-05-2 HCAPLUS  
 CN Benzoic acid, 2-[(4-phenyl-1-piperidinyl)sulfonyl]- (9CI) (CA INDEX NAME)



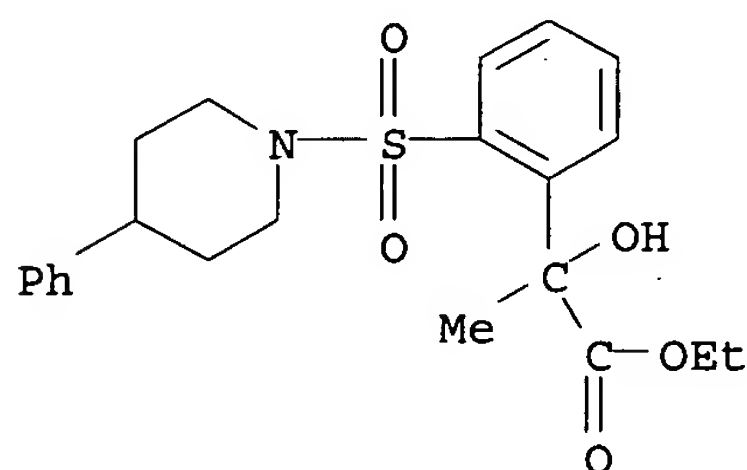
RN 308386-06-3 HCAPLUS

CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)



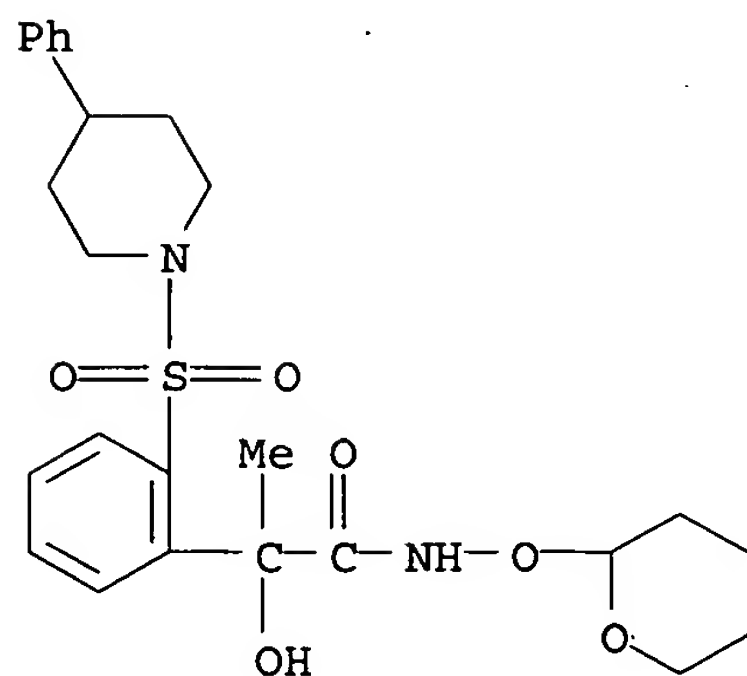
RN 308386-07-4 HCAPLUS

CN Benzeneacetic acid,  $\alpha$ -hydroxy- $\alpha$ -methyl-2-[(4-phenyl-1-piperidinyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 308386-08-5 HCAPLUS

CN Benzeneacetamide,  $\alpha$ -hydroxy- $\alpha$ -methyl-2-[(4-phenyl-1-piperidinyl)sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



IT 308385-92-4P

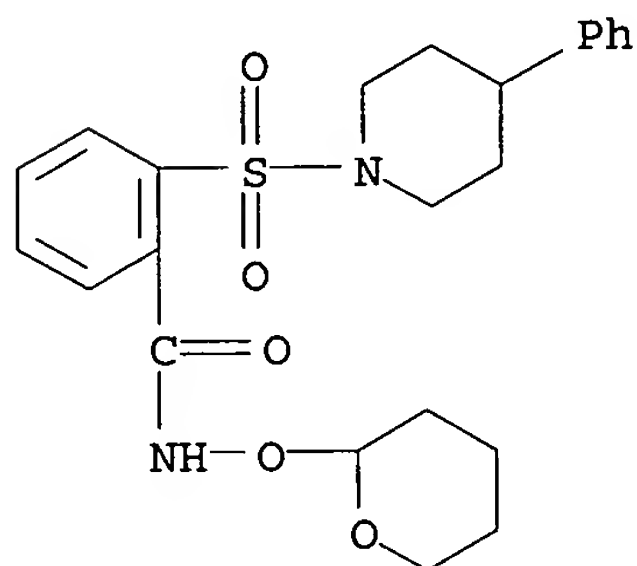
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
USES (Uses)

(preparation of hydroxamic acid derivs. as matrix metalloprotease  
**inhibitors**)

RN 308385-92-4 HCAPLUS

CN Benzamide, 2-[(4-phenyl-1-piperidiny]sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



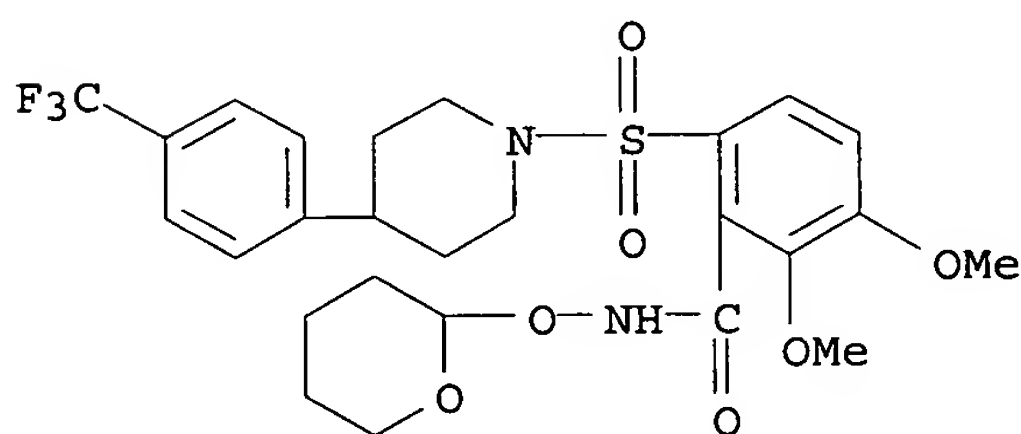
IT 308385-98-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acid derivs. as matrix metalloprotease  
**inhibitors**)

RN 308385-98-0 HCAPLUS

CN Benzamide, 2,3-dimethoxy-N-[(tetrahydro-2H-pyran-2-yl)oxy]-6-[[4-[4-(trifluoromethyl)phenyl]-1-piperidiny]sulfonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:535116 HCAPLUS

DOCUMENT NUMBER: 133:150472

TITLE: Preparation of alkynyloxyphenylsulfonylmethylpiperidin  
ehydroxamic acids and related compounds as  
**inhibitors** of matrix metalloprotease and  
TNF- $\alpha$  converting **enzyme** (TACE).

INVENTOR(S): Levin, Jeremy Ian; Venkatesan, Aranapakam Mudumbai;  
Chen, James Ming; Zask, Arie; Sandanayaka, Vincent  
Premarana; Du, Mila Ti; Baker, Jannie Lea

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 136 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044723	A1	20000803	WO 2000-US1864	20000127 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356313	AA	20000803	CA 2000-2356313	20000127 <--
EP 1147085	A1	20011024	EP 2000-904569	20000127 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000007784	A	20020205	BR 2000-7784	20000127 <--
JP 2002535390	T2	20021022	JP 2000-595979	20000127 <--
AU 769418	B2	20040129	AU 2000-26305	20000127
NZ 512566	A	20040227	NZ 2000-512566	20000127
ZA 2001005222	A	20020925	ZA 2001-5222	20010625 <--
NO 2001003678	A	20010920	NO 2001-3678	20010726 <--
PRIORITY APPLN. INFO.:			US 1999-238038	A 19990127
			WO 2000-US1864	W 20000127

OTHER SOURCE(S): MARPAT 133:150472

AB R1C.tplbond.CCR2R3XYACR8R9(CR10R11)nCONR12OH (R1 = H, aryl, heteroaryl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloheteroalkyl; R2, R3 = H, alkyl, cyano, CCH; R8-R11 = H, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, alkyl, alkenyl, alkynyl; 1 of R8R9, R9R10, or R10R11 = atoms to form a cycloalkyl ring or a cycloheteroalkyl ring; R12 = H, aryl, heteroaryl, cycloalkyl, cycloheteroalkyl, alkyl; A, X = O, S, SO, SO2, NR7, CH2; R7 = H, aryl, aralkyl, heteroaryl, heteroaralkyl, etc.; Y = aryl, heteroaryl; A and X are not bonded to adjacent atoms of Y; n = 0-2), were prepared Thus, 1-acetyl-4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-4-piperidinecarboxamide (preparation in several steps from Et isonipecotate given) inhibited TACE with IC50 = 4.8 nM.

IT 287201-30-3P

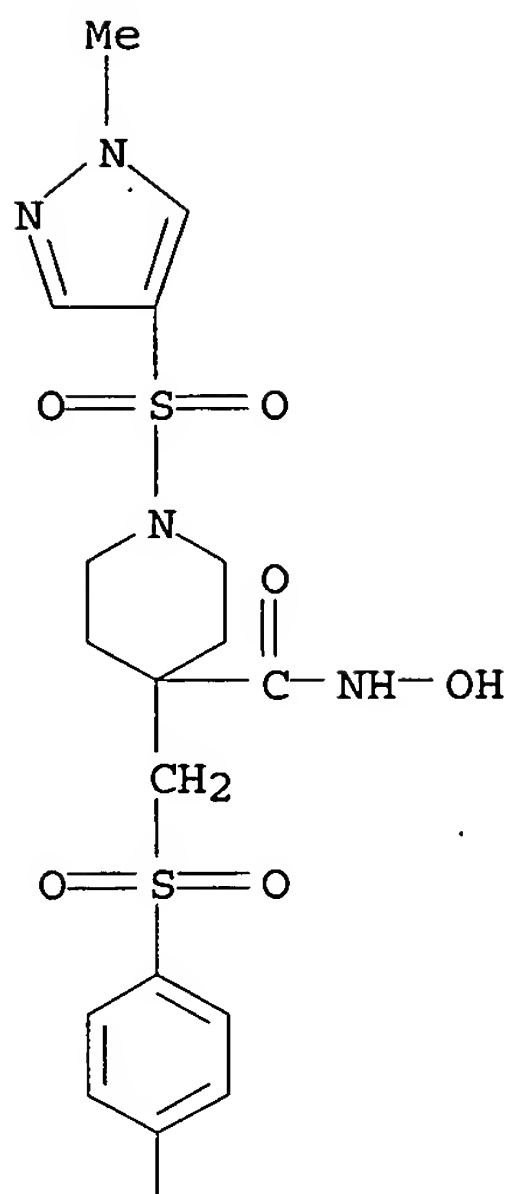
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of alkynyloxyphenylsulfonylmethylpiperidinehydroxamic acids and related compds. as inhibitors of matrix metalloproteinase and TNF- $\alpha$  converting enzyme (TACE))

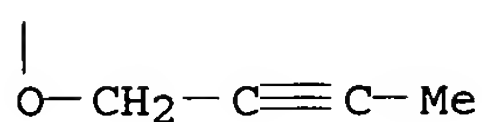
RN 287201-30-3 HCAPLUS

CN 4-Piperidinecarboxamide, 4-[[[4-(2-butynyloxy)phenyl]sulfonyl]methyl]-N-hydroxy-1-[(1-methyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



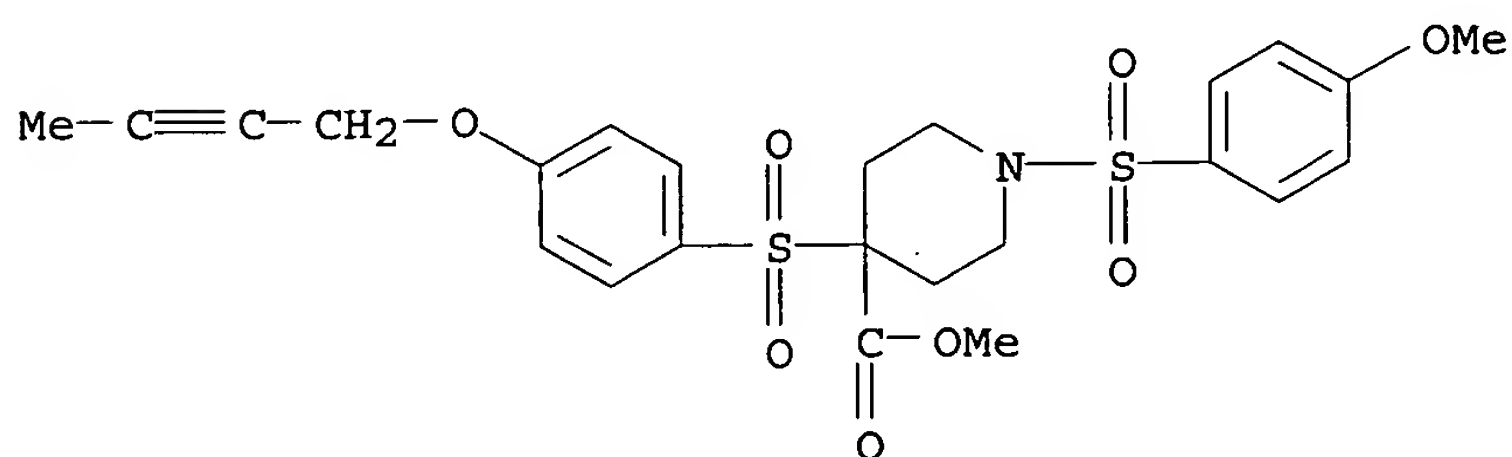
IT 287202-66-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of alkynyloxyphenylsulfonylmethylpiperidinehydroxamic acids and related compds. as **inhibitors** of matrix metalloproteinase and TNF- $\alpha$  converting **enzyme** (TACE))

RN 287202-66-8 HCAPLUS

CN 4-Piperidinecarboxylic acid, 4-[[4-(2-butynyloxy)phenyl]sulfonyl]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



L32 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:535102 HCAPLUS

DOCUMENT NUMBER: 133:150908

TITLE: Preparation of acetylenic  $\alpha$ -amino acid-based  
sulfonamide hydroxamic acid TACE inhibitors

INVENTOR(S): Levin, Jeremy Ian; Chen, James Ming; Cole, Derek Cecil

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 293 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044709	A2	20000803	WO 2000-US1981	20000127 <--
WO 2000044709	A3	20001221		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356299	AA	20000803	CA 2000-2356299	20000127 <--
EP 1144368	A2	20011017	EP 2000-905750	20000127 <--
EP 1144368	B1	20040714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000007752	A	20011204	BR 2000-7752	20000127 <--
TR 200102132	T2	20020121	TR 2001-200102132	20000127 <--
JP 2002535382	T2	20021022	JP 2000-595966	20000127 <--
AU 766717	B2	20031023	AU 2000-27384	20000127 <--
NZ 511928	A	20031128	NZ 2000-511928	20000127 <--
TW 593247	B	20040621	TW 2000-89101287	20000127
AT 271035	E	20040715	AT 2000-905750	20000127
PT 1144368	T	20040930	PT 2000-905750	20000127
ES 2225089	T3	20050316	ES 2000-905750	20000127
ZA 2001004326	A	20020826	ZA 2001-4326	20010525 <--
NO 2001003674	A	20010924	NO 2001-3674	20010726 <--
BG 105738	A	20020531	BG 2001-105738	20010726 <--
HK 1038735	A1	20050107	HK 2002-100184	20020110
PRIORITY APPLN. INFO.:			US 1999-238255	A 19990127
			WO 2000-US1981	W 20000127

OTHER SOURCE(S): MARPAT 133:150908

AB Amino acid derivs. HONHCOCR1R2NR3-X-Y-Z-CR4R5C.tplbond.CR6 [X = SO<sub>2</sub>, P(O)R<sub>10</sub>, where R<sub>10</sub> = alkyl, cycloalkyl, aryl, heteroaryl; Y = aryl, heteroaryl, with the proviso that X and Z may not be bonded to adjacent atoms of Y; Z = O, NH, CH<sub>2</sub>, S; R<sub>1</sub> = H, aryl, alkyl, alkenyl, alkynyl; R<sub>2</sub> = any group given for R<sub>1</sub>, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloheteroalkyl or R<sub>1</sub> and R<sub>2</sub> may form a ring; R<sub>3</sub> = H, alkyl, cycloalkyl, cycloheteroalkyl, aralkyl, heteroaralkyl or R<sub>1</sub> and R<sub>3</sub> may form a ring; R<sub>4</sub>, R<sub>5</sub> = H, alkyl, CN, C.tplbond.CH; R<sub>6</sub> = any group given for R<sub>1</sub>, heteroaryl, cycloalkyl, cycloheteroalkyl] or pharmaceutically acceptable salts were prepared as inhibitors of TNF- $\alpha$  converting enzyme (TACE). Thus, 2-[(4-but-2-ynyloxybenzenesulfonyl)methylamino]-N-hydroxy-3-

methylbutyramide was prepared and showed IC50 = 7.4 nM for inhibition of TACE.

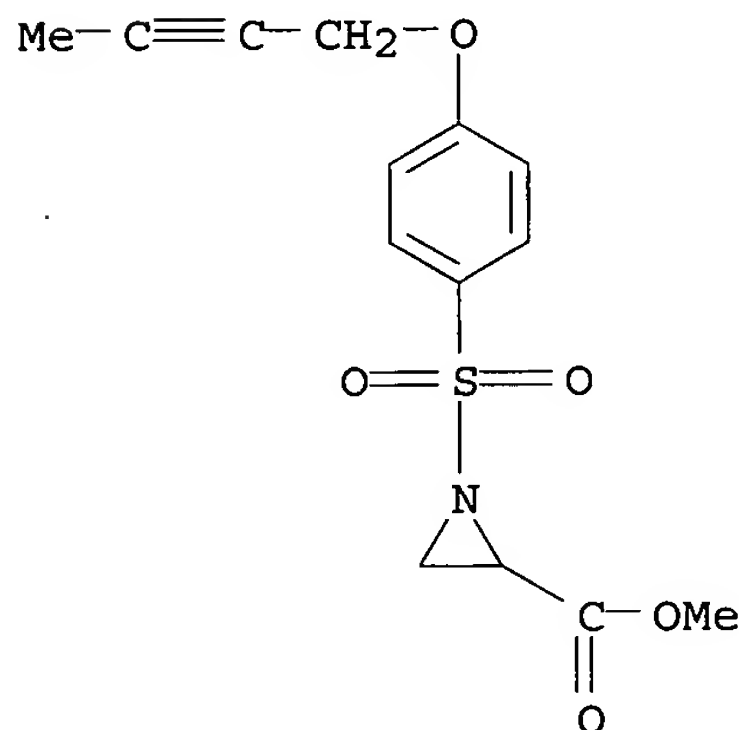
IT 287408-00-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of acetylenic  $\alpha$ -amino acid-based sulfonamide hydroxamic acid TACE inhibitors)

RN 287408-00-8 HCAPLUS

CN 2-Aziridinecarboxylic acid, 1-[[4-(2-butyloxy)phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



L32 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:819347 HCAPLUS

DOCUMENT NUMBER: 132:64103

TITLE: Preparation of amidino and guanidino azetidinone compounds as tryptase inhibitors

INVENTOR(S): Bisacchi, Gregory; Slusarchyk, William A.; Treuner, Uwe; Sutton, James C.; Zahler, Robert; Seiler, Steven; Kronenthal, David R.; Randazzo, Michael E.; Xu, Zhongmin; Shi, Zhongping; Schwinden, Mark D.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA

SOURCE: PCT Int. Appl., 326 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

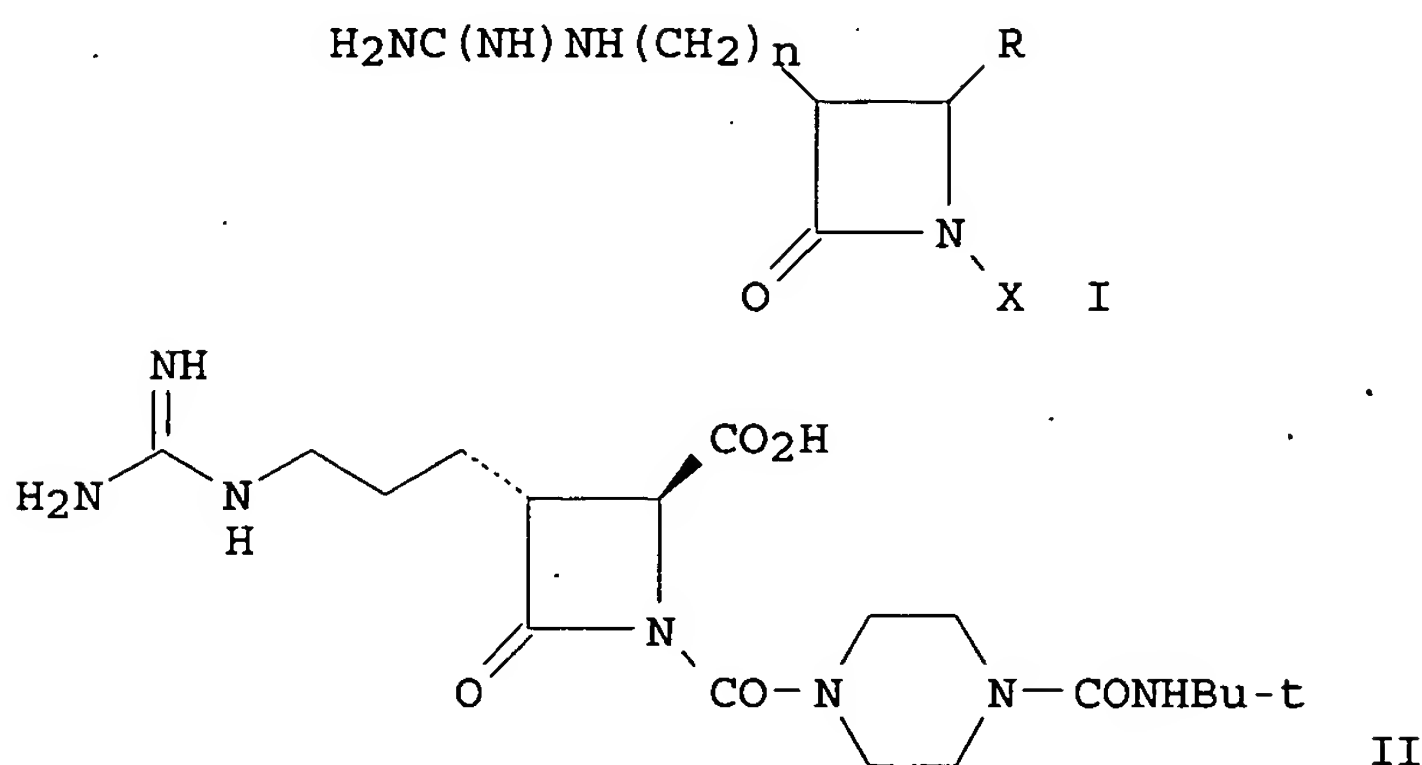
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967215	A1	19991229	WO 1999-US13811	19990618 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2336003	AA	19991229	CA 1999-2336003	19990618 <--
AU 9946950	A1	20000110	AU 1999-46950	19990618 <--

AU 752320	B2	20020912		
EP 1089973	A1	20010411	EP 1999-930402	19990618 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TR 200003859	T2	20010723	TR 2000-200003859	19990618 <--
BR 9911373	A	20010918	BR 1999-11373	19990618 <--
JP 2002518478	T2	20020625	JP 2000-555869	19990618 <--
RU 2211832	C2	20030910	RU 2001-102266	19990618 <--
NZ 507627	A	20031219	NZ 1999-507627	19990618
TW 548270	B	20030821	TW 1999-88110361	19990621 <--
ZA 2000006028	A	20020725	ZA 2000-6028	20001025 <--
NO 2000006380	A	20001214	NO 2000-6380	20001214 <--
PRIORITY APPLN. INFO.:			US 1998-90636P	P 19980625
			WO 1999-US13811	W 19990618
OTHER SOURCE(S):		MARPAT 132:64103		
GI				

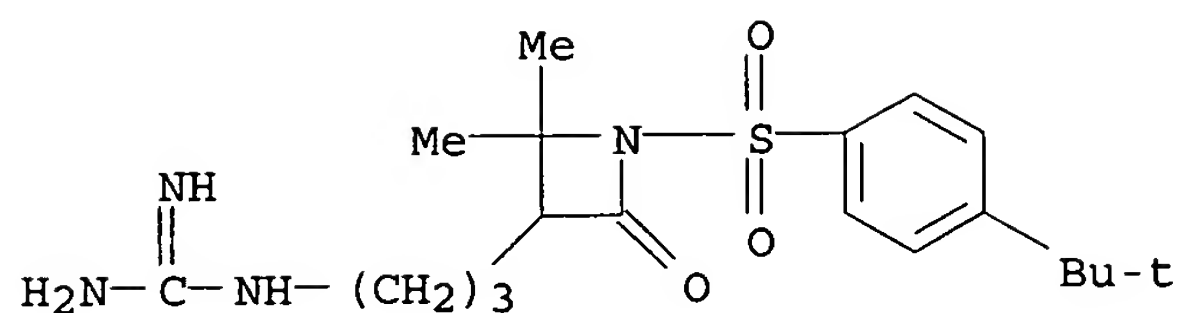


AB Novel  $\beta$ -lactam compds., e.g. of formula I [R - CO<sub>2</sub>H, CONH-alkyl, etc.; X = CONH(CH<sub>2</sub>)<sub>2</sub>NHCO<sub>2</sub>alkyl, etc.; n = 1-6;], are prepared as **inhibitors** of in vivo **enzyme** systems including tryptase, thrombin, trypsin, factor Xa, factor VIIa, and urokinase-type plasminogen activator (no data). The tryptase activity makes the title compds. useful as antiinflammatory agents in the treatment of chronic asthma and allergic rhinitis. Thus, II was prepared from (4S)-N-(tert-butyltrimethylsilyl)azetidin-2-one-4-carboxylic acid, tert-butyl-1-piperazine carboxylate and tert-Bu isocyanate.

IT 253174-33-3P 253174-35-5P 253174-36-6P  
253174-39-9P 253174-40-2P 253174-53-7P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of amidino and guanidino azetidinone compds. as tryptase **inhibitors**)

RN 253174-33-3 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]-4,4-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

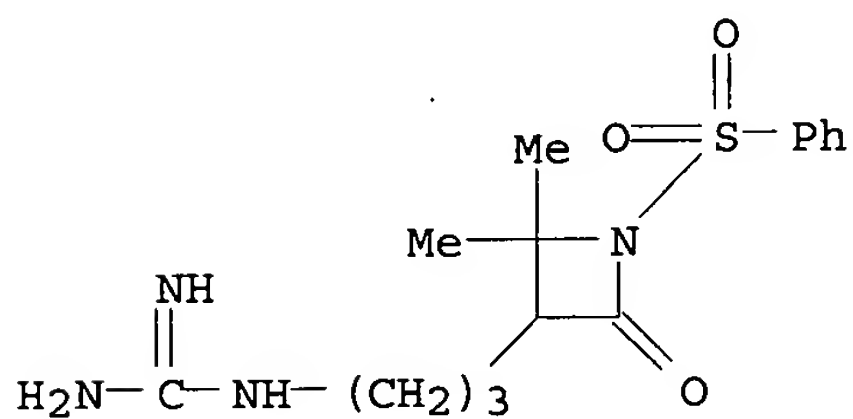
RN 253174-35-5 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 253174-34-4

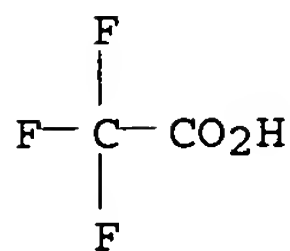
CMF C15 H22 N4 O3 S



CM 2

CRN 76-05-1

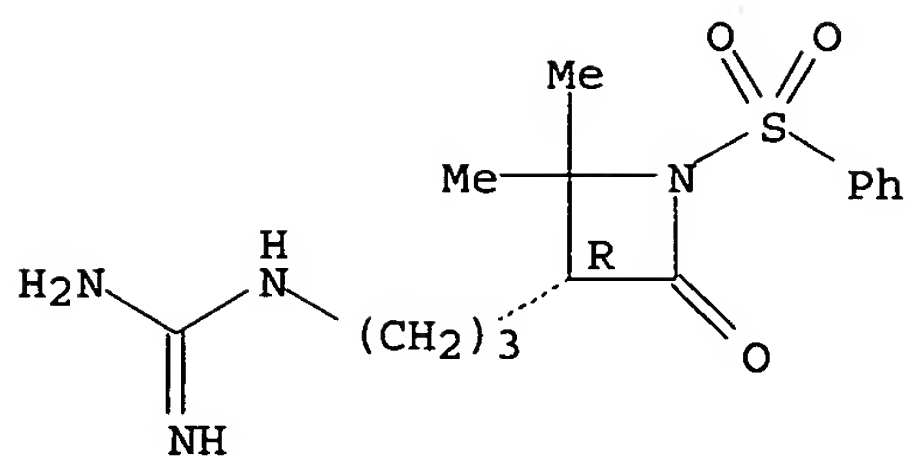
CMF C2 H F3 O2



RN 253174-36-6 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

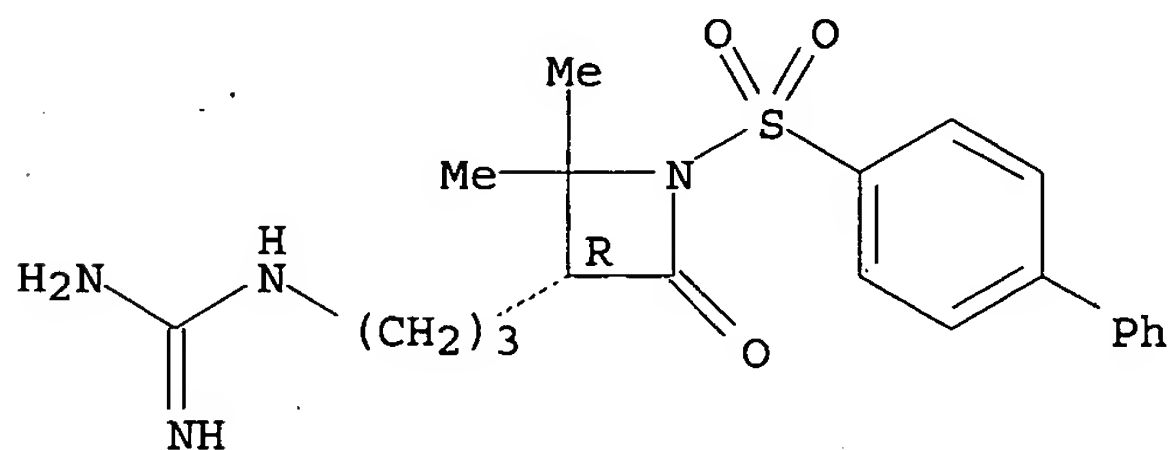


● HCl

RN 253174-39-9 HCAPLUS

CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-1-([1,1'-biphenyl]-4-ylsulfonyl)-4,4-dimethyl-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

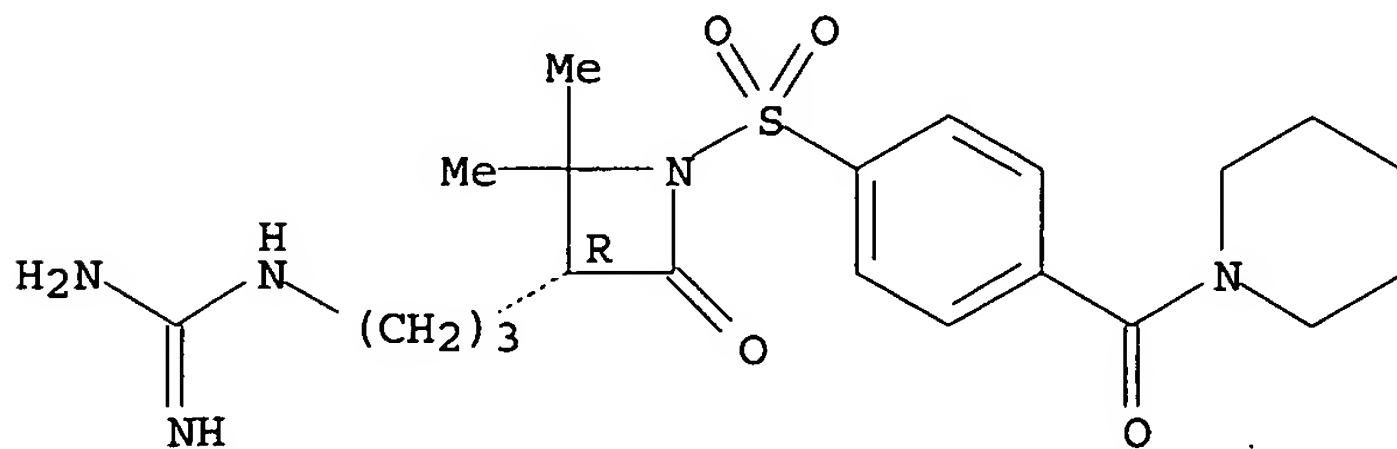


● HCl

RN 253174-40-2 HCAPLUS

CN Piperidine, 1-[4-[[[(3R)-3-[3-[(aminoiminomethyl)amino]propyl]-2,2-dimethyl-4-oxo-1-azetidinyl]sulfonyl]benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 253174-53-7 HCAPLUS

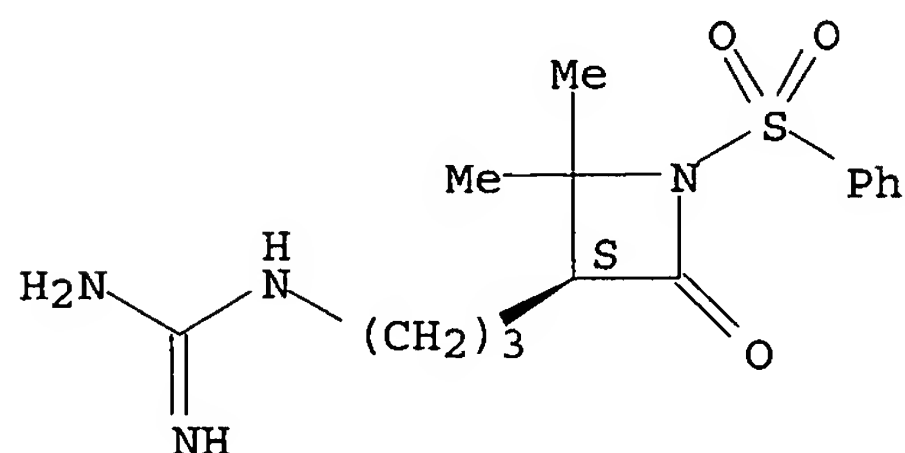
CN 2-Azetidinone, 3-[3-[(aminoiminomethyl)amino]propyl]-4,4-dimethyl-1-(phenylsulfonyl)-, (3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 253174-52-6

CMF C15 H22 N4 O3 S

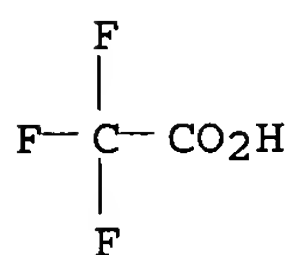
Absolute stereochemistry. Rotation (-).



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 253176-09-9P 253176-75-9P 253176-76-0P

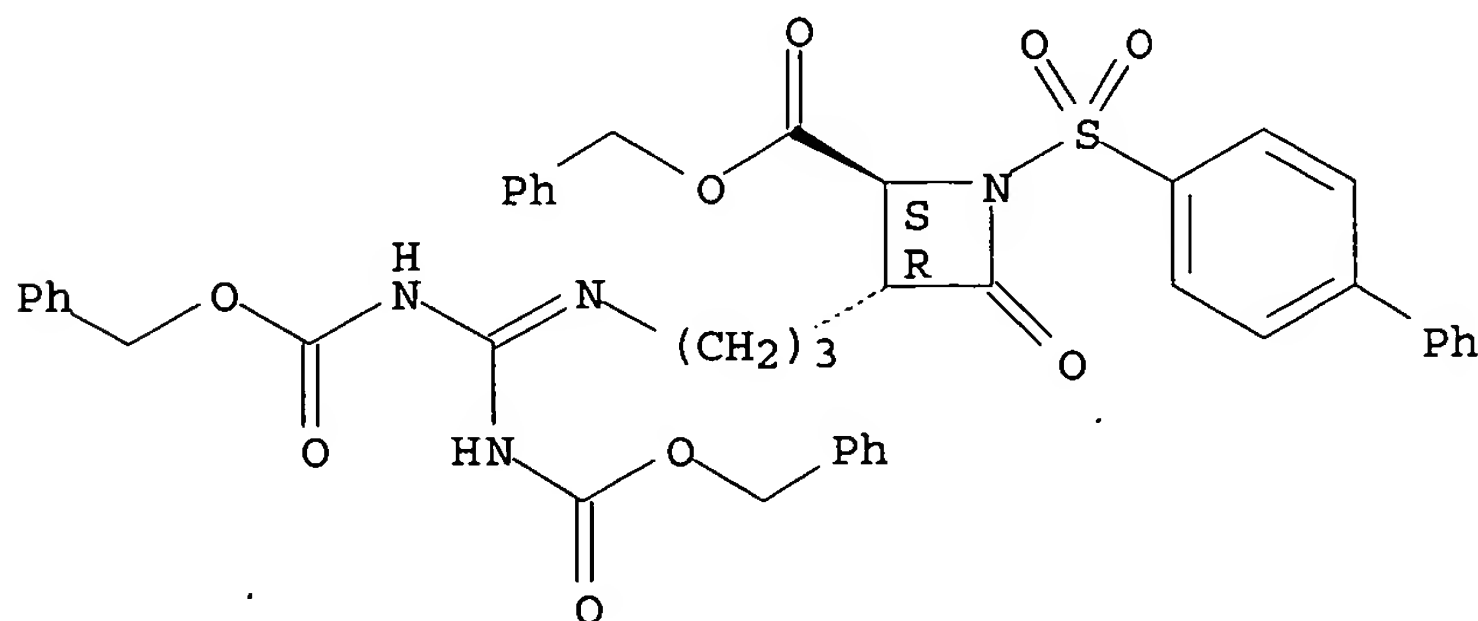
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidino and guanidino azetidinone compds. as tryptase inhibitors)

RN 253176-09-9 HCAPLUS

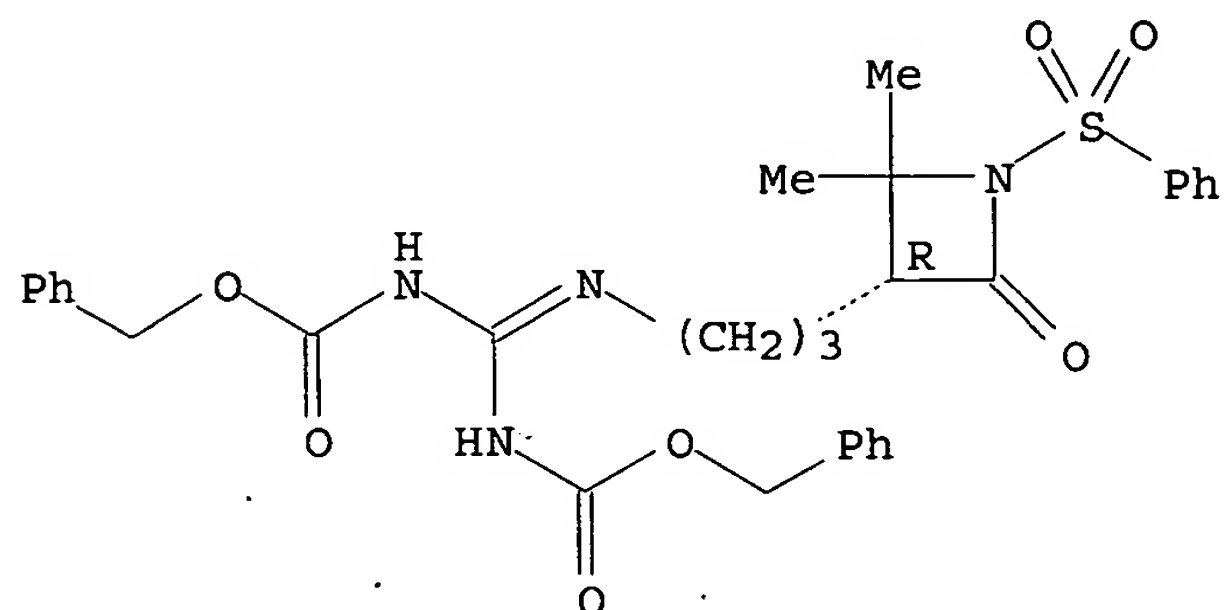
CN 2-Azetidinecarboxylic acid, 1-([1,1'-biphenyl]-4-ylsulfonyl)-3-[3-[[bis[(phenylmethoxy)carbonyl]amino]methylene]amino]propyl]-4-oxo-, phenylmethyl ester, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



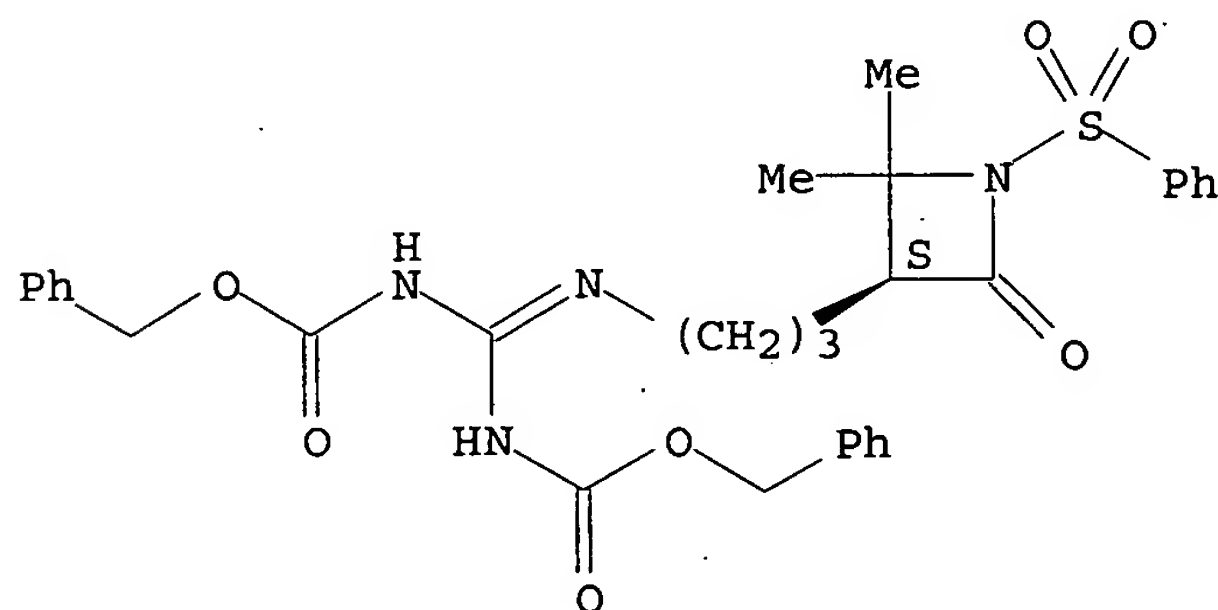
RN 253176-75-9 HCAPLUS  
 CN Carbamic acid, [[3-[(3R)-2,2-dimethyl-4-oxo-1-(phenylsulfonyl)-3-azetidinyl]propyl]carbonimidoyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 253176-76-0 HCAPLUS  
 CN Carbamic acid, [[3-[(3S)-2,2-dimethyl-4-oxo-1-(phenylsulfonyl)-3-azetidinyl]propyl]carbonimidoyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:672748 HCAPLUS

DOCUMENT NUMBER: 131:299363

TITLE: Substituted pyrrolidine hydroxamate metalloprotease inhibitors

INVENTOR(S): Cheng, Menyan; Natchus, Michael George; De, Biswanath; Almstead, Neil Gregory; Taiwo, Yetunde Olabisi; Pikul, Stanislaw

PATENT ASSIGNEE(S): The Procter & Gamble Company, USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

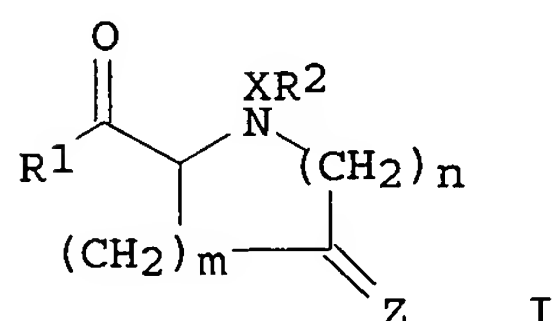
FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952868	A1	19991021	WO 1999-US7826	19990409 <--
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6329418	B1	20011211	US 1999-274564	19990323 <--
CA 2328211	AA	19991021	CA 1999-2328211	19990409 <--
AU 9935522	A1	19991101	AU 1999-35522	19990409 <--
AU 753048	B2	20021003		
BR 9909620	A	20001219	BR 1999-9620	19990409 <--
EP 1073635	A1	20010207	EP 1999-917387	19990409 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
TR 200002971	T2	20010221	TR 2000-200002971	19990409 <--
JP 2002511448	T2	20020416	JP 2000-543431	19990409 <--
NZ 507076	A	20030429	NZ 1999-507076	19990409 <--
ZA 2000005047	A	20010606	ZA 2000-5047	20000921 <--
NO 2000005196	A	20001214	NO 2000-5196	20001016 <--
PRIORITY APPLN. INFO.:			US 1998-81667P	P 19980414
			WO 1999-US7826	W 19990409

OTHER SOURCE(S): MARPAT 131:299363

GI



AB Title compds. I [R1 = OH, alkoxy, (un)substituted NHOH; X = SO<sub>2</sub>, CO, CO<sub>2</sub>, (un)substituted CONH, POH; R<sub>2</sub> = H, alkyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aryloxy, heteroaryloxy; Z = (un)substituted NH, CH<sub>2</sub>; m, n = 0-4] are potent **inhibitors** of metalloproteases (no data) and are effective in treating conditions characterized by excess activity of these **enzymes**. Thus, cis-hydroxy-D-proline was treated with 4-MeOC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl, esterified, oxidized to the ketone, and treated with NH<sub>2</sub>OK to give I [R1 = NHOH, XR<sub>2</sub> = SO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>OMe-4, Z = NOH, m, n = 1].

IT 203934-42-3P 203934-63-8P 203934-64-9P  
 203994-80-3P 204072-55-9P 247058-60-2P  
 247058-61-3P 247058-62-4P 247058-63-5P  
 247058-64-6P 247058-65-7P 247058-67-9P  
 247058-68-0P 247058-70-4P 247058-71-5P  
 247058-72-6P 247058-73-7P 247058-74-8P  
 247058-75-9P 247058-76-0P 247058-77-1P  
 247058-78-2P 247058-79-3P 247058-80-6P  
 247058-81-7P 247058-82-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT



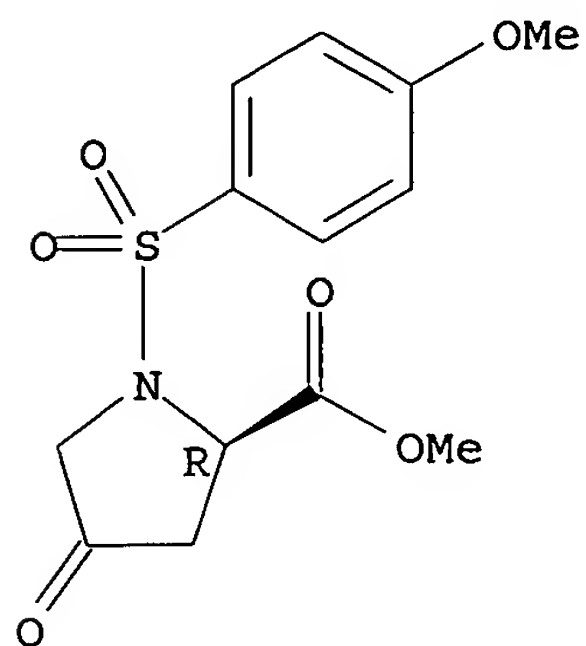
(Reactant or reagent)

(preparation of arylsulfonylpyrrolidinecarboxylates as metalloprotease inhibitors)

RN 203934-42-3 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

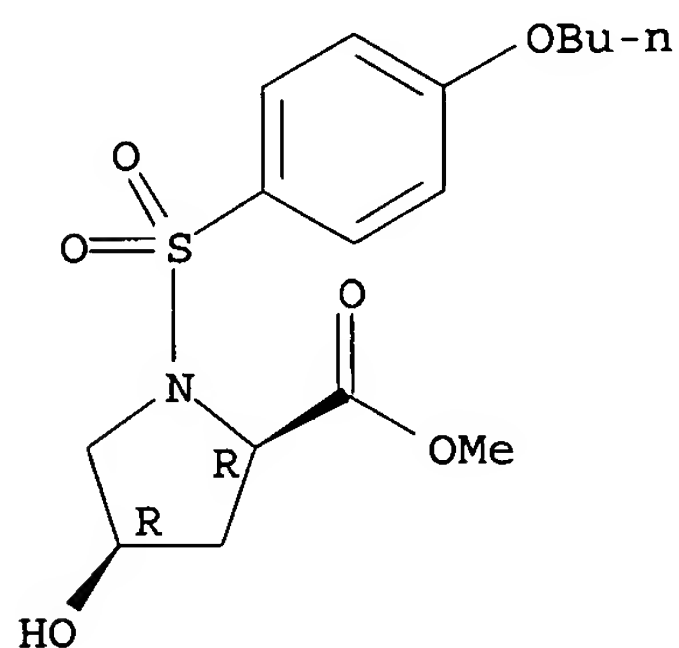
Absolute stereochemistry.



RN 203934-63-8 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-hydroxy-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

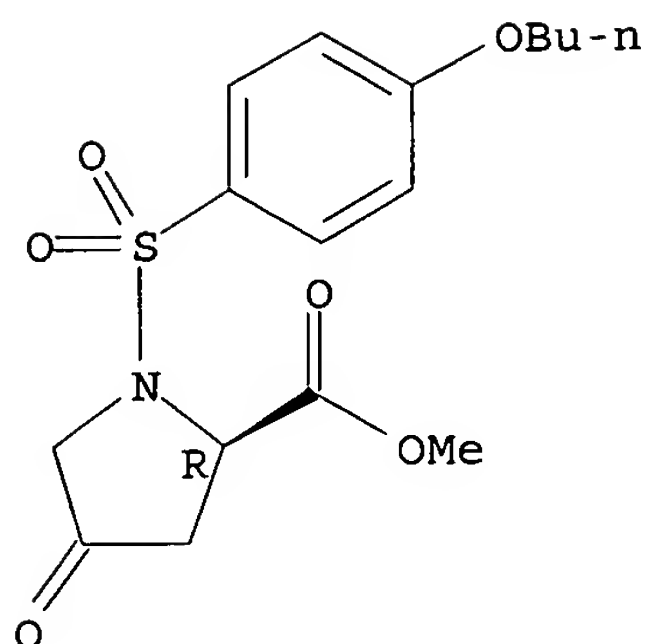
Absolute stereochemistry.



RN 203934-64-9 HCAPLUS

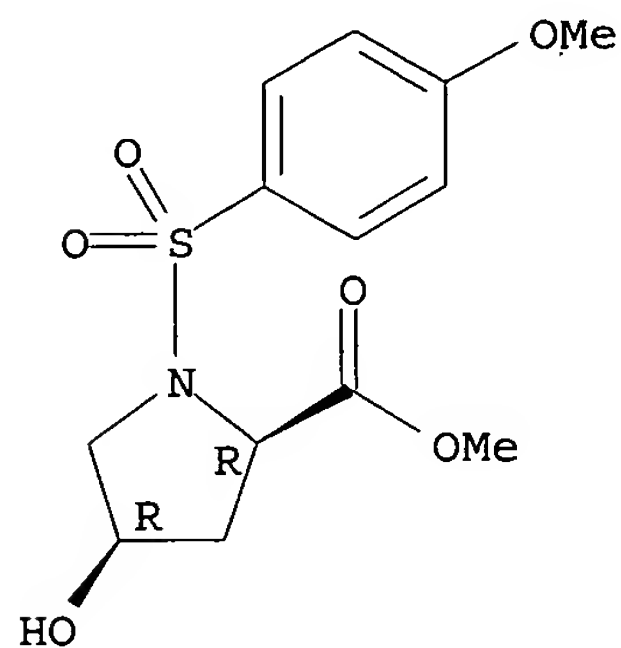
CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



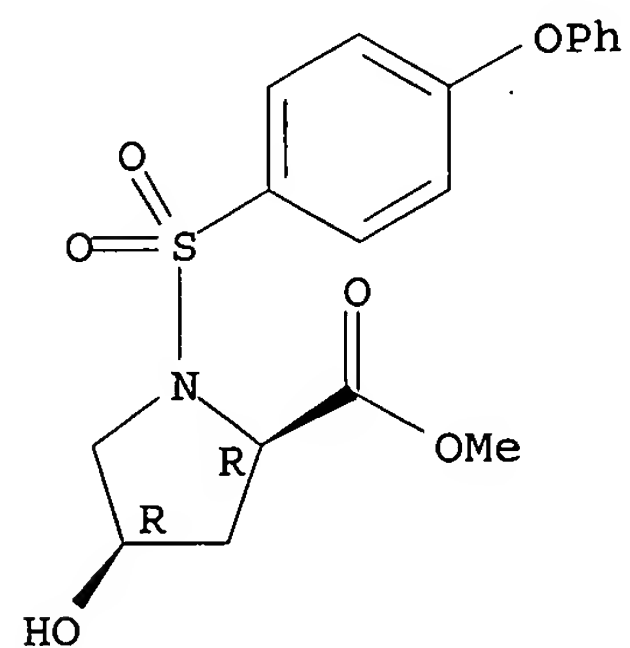
RN 203994-80-3 HCAPLUS  
 CN D-Proline, 4-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester, (4R)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204072-55-9 HCAPLUS  
 CN D-Proline, 4-hydroxy-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester, (4R)-  
 (9CI) (CA INDEX NAME)

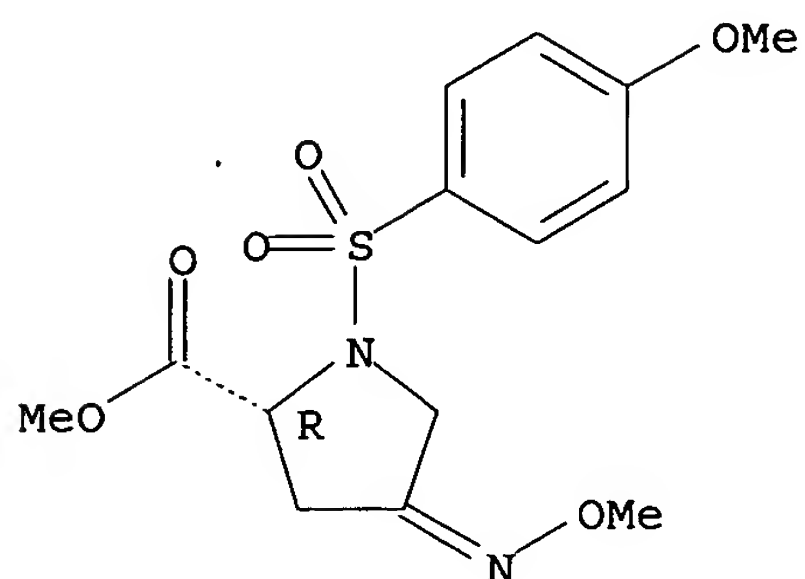
Absolute stereochemistry.



RN 247058-60-2 HCAPLUS  
 CN D-Proline, 4-(methoxyimino)-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

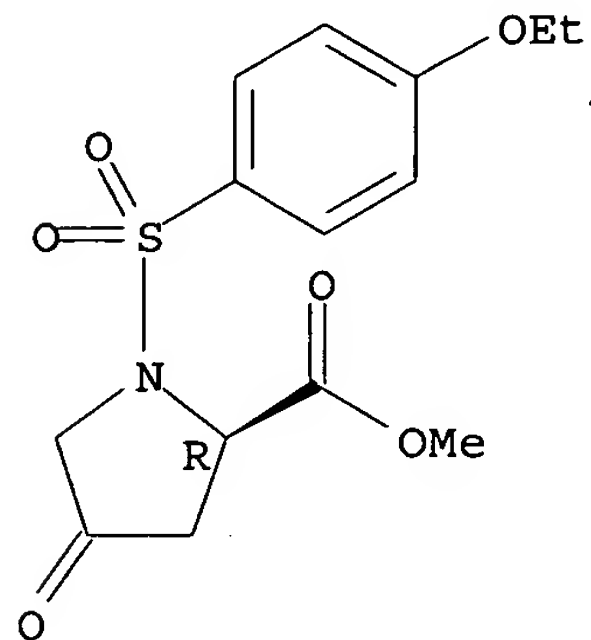
Double bond geometry unknown.



RN 247058-61-3 HCAPLUS

CN D-Proline, 1-[(4-ethoxyphenyl)sulfonyl]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

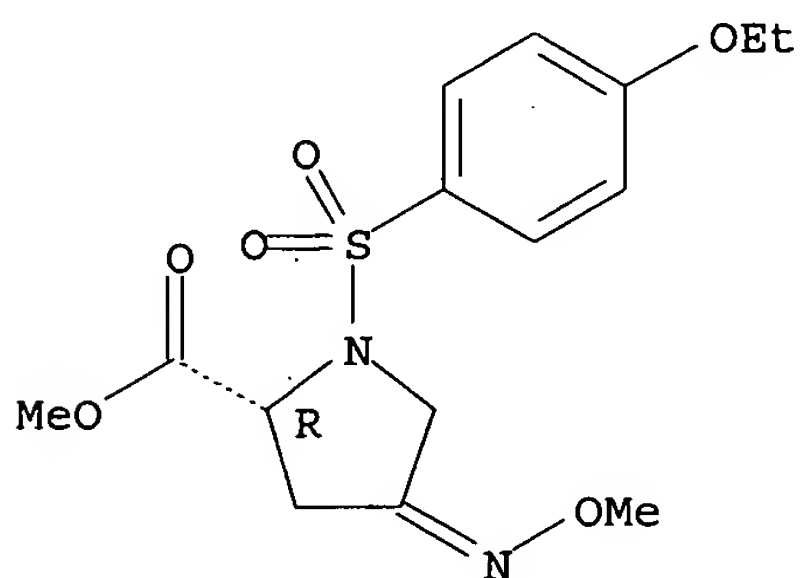


RN 247058-62-4 HCAPLUS

CN D-Proline, 1-[(4-ethoxyphenyl)sulfonyl]-4-(methoxyimino)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

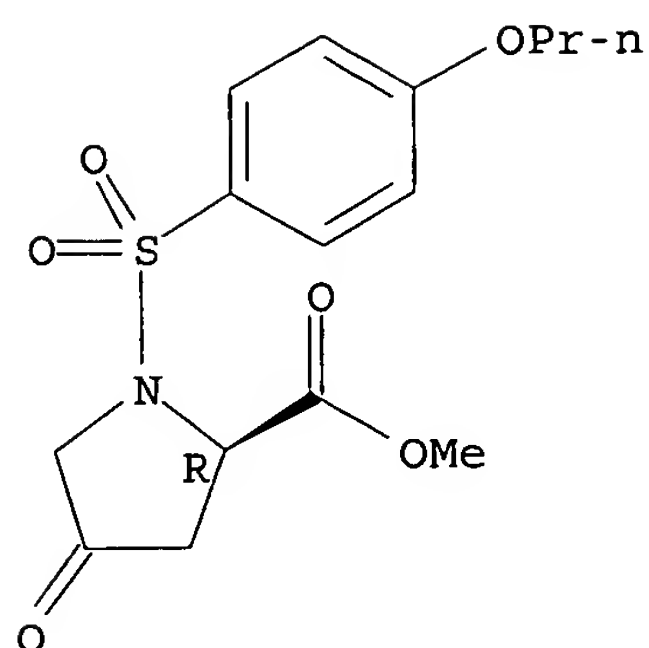
Double bond geometry unknown.



RN 247058-63-5 HCAPLUS

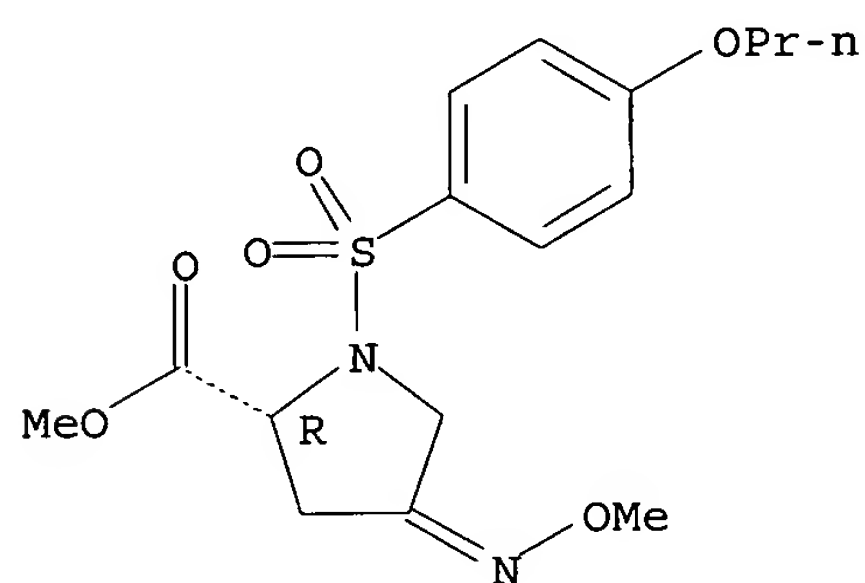
CN D-Proline, 4-oxo-1-[(4-propoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



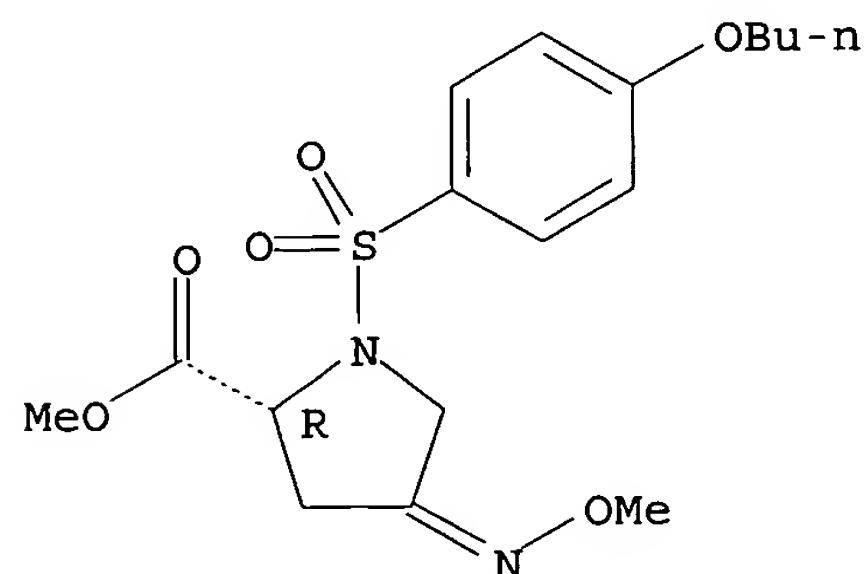
RN 247058-64-6 HCAPLUS  
 CN D-Proline, 4-(methoxyimino)-1-[(4-propoxyphenyl)sulfonyl]-, methyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



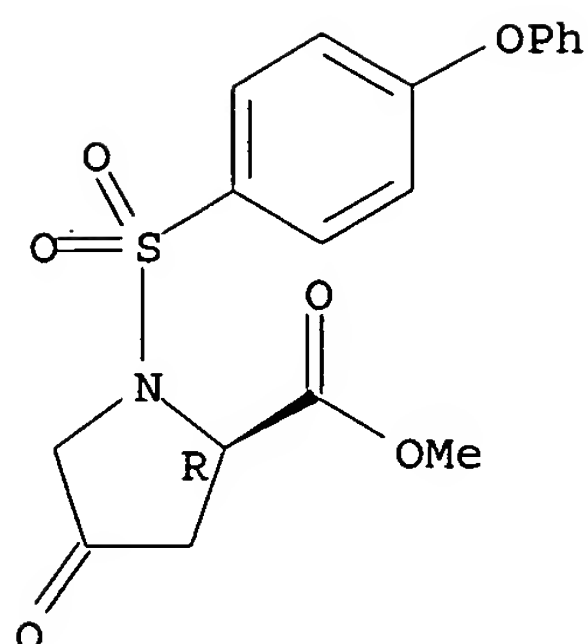
RN 247058-65-7 HCAPLUS  
 CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(methoxyimino)-, methyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



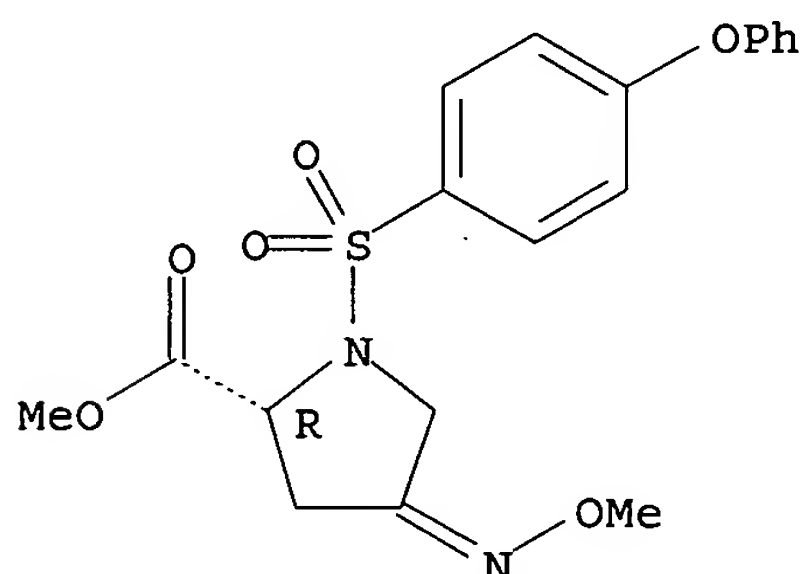
RN 247058-67-9 HCAPLUS  
 CN D-Proline, 4-oxo-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



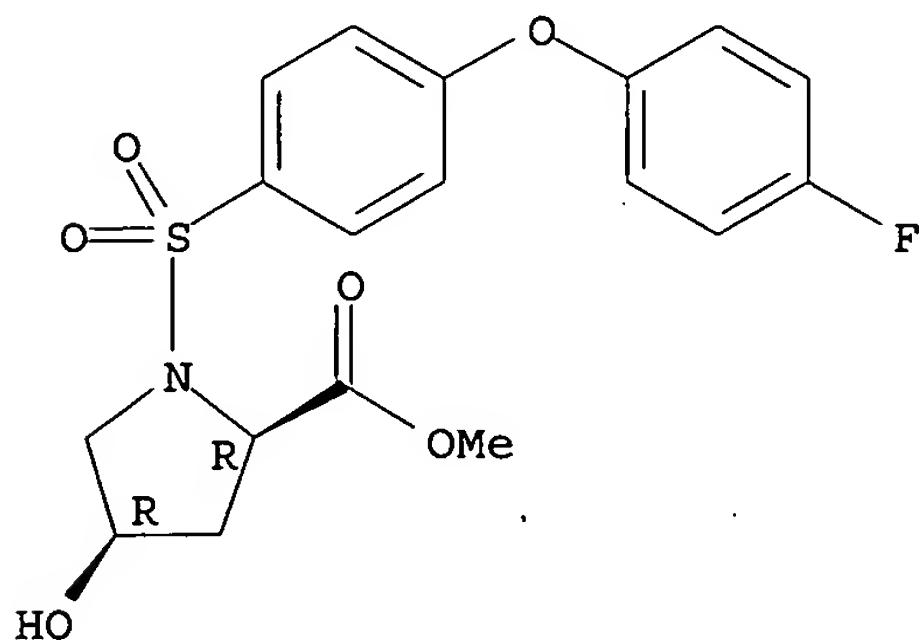
RN 247058-68-0 HCAPLUS  
 CN D-Proline, 4-(methoxyimino)-1-[(4-phenoxyphenyl)sulfonyl]-, methyl ester  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



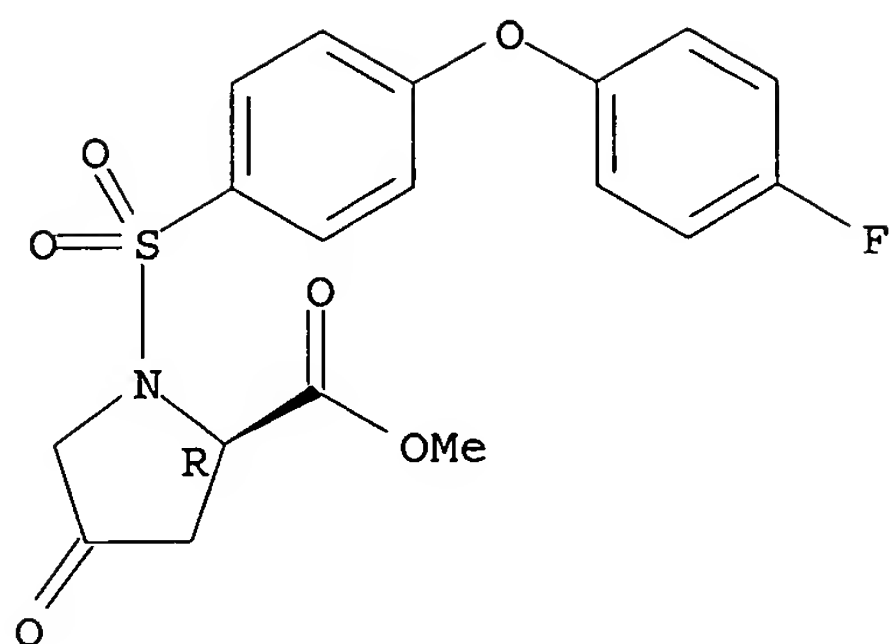
RN 247058-70-4 HCAPLUS  
 CN D-Proline, 1-[[4-(4-fluorophenoxy)phenyl]sulfonyl]-4-hydroxy-, methyl  
 ester, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247058-71-5 HCAPLUS  
 CN D-Proline, 1-[[4-(4-fluorophenoxy)phenyl]sulfonyl]-4-oxo-, methyl ester  
 (9CI) (CA INDEX NAME)

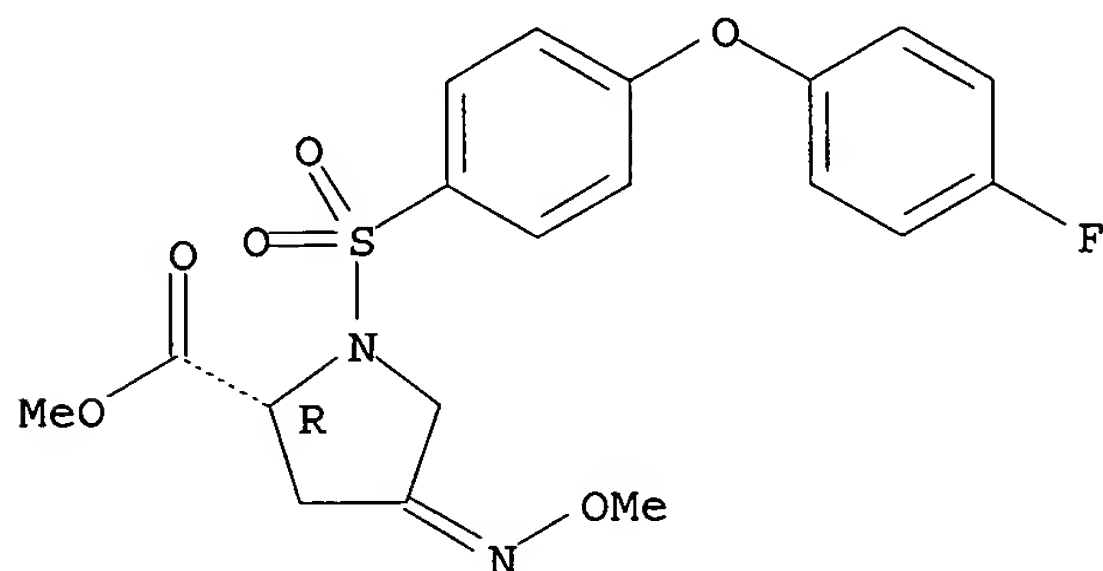
Absolute stereochemistry.



RN 247058-72-6 HCAPLUS

CN D-Proline, 1-[[4-(4-fluorophenoxy)phenyl]sulfonyl]-4-(methoxyimino)-, methyl ester (9CI) (CA INDEX NAME)

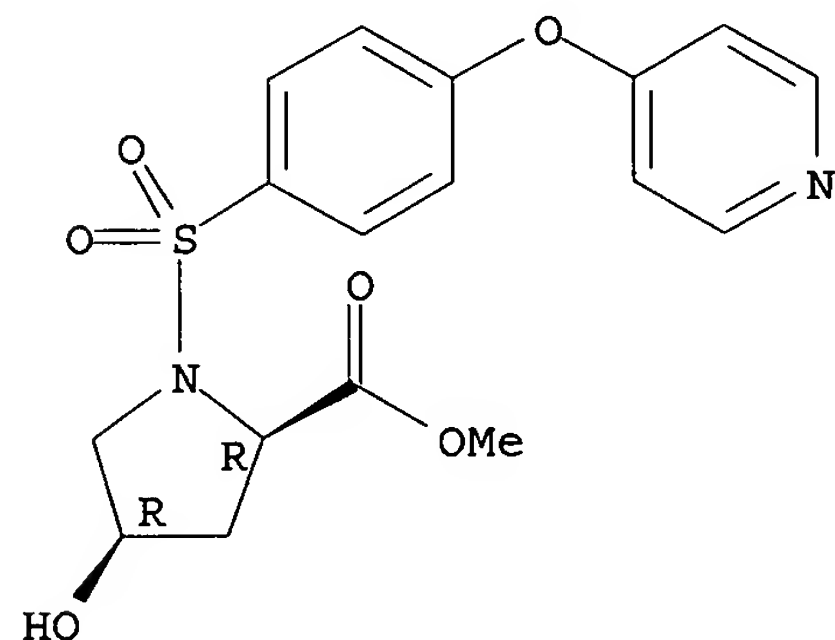
Absolute stereochemistry.  
Double bond geometry unknown.



RN 247058-73-7 HCAPLUS

CN D-Proline, 4-hydroxy-1-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

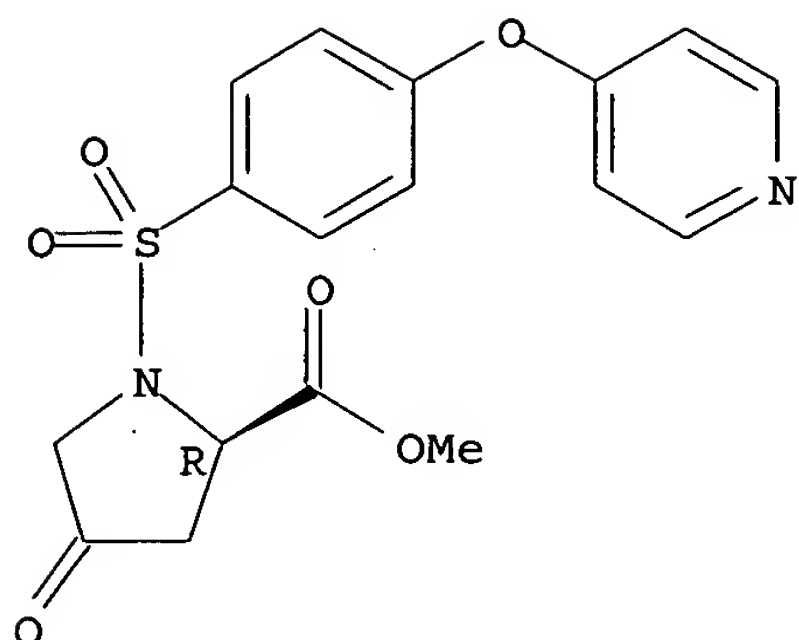
Absolute stereochemistry.



RN 247058-74-8 HCAPLUS

CN D-Proline, 4-oxo-1-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

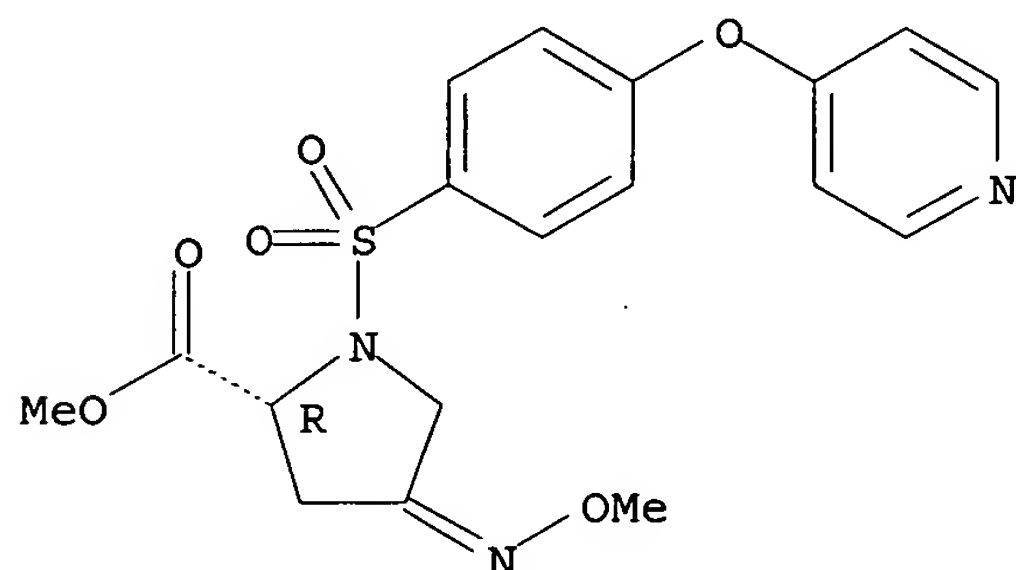
Absolute stereochemistry.



RN 247058-75-9 HCAPLUS

CN D-Proline, 4-(methoxyimino)-1-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

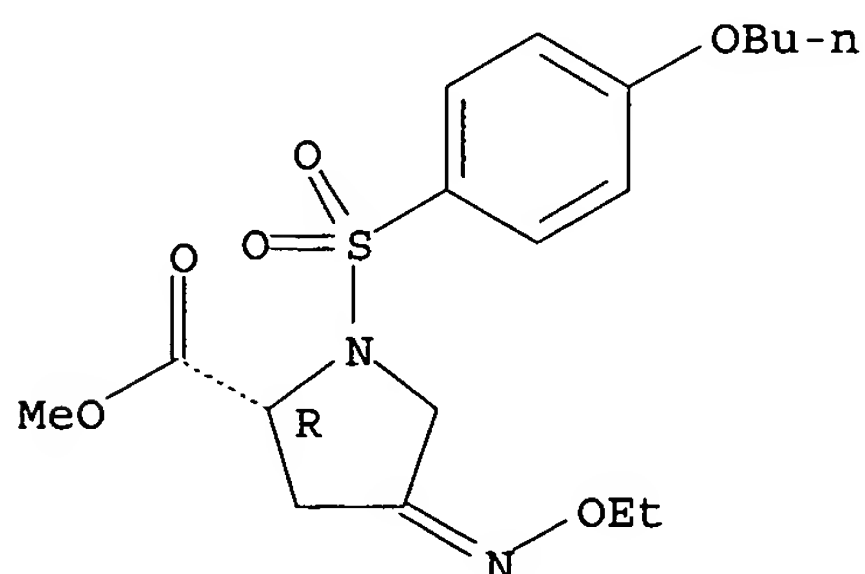
Absolute stereochemistry.  
Double bond geometry unknown.



RN 247058-76-0 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(ethoxyimino)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

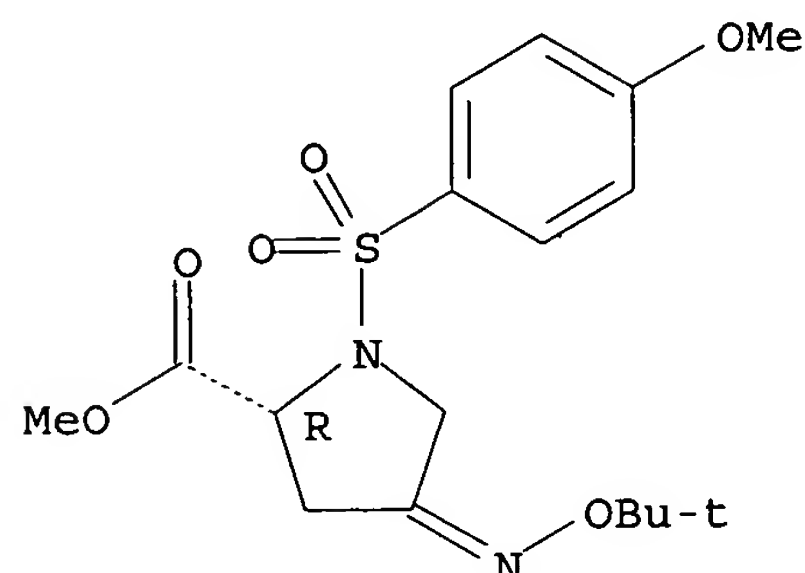


RN 247058-77-1 HCAPLUS

CN D-Proline, 4-[(1,1-dimethylethoxy)imino]-1-[(4-methoxyphenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

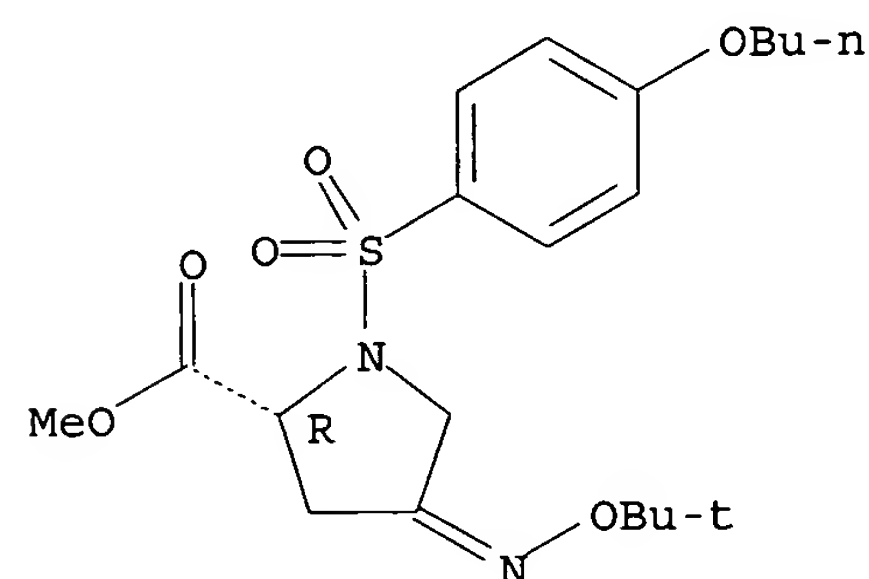
Double bond geometry unknown.



RN 247058-78-2 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-[(1,1-dimethylethoxy)imino]-, methyl ester (9CI) (CA INDEX NAME)

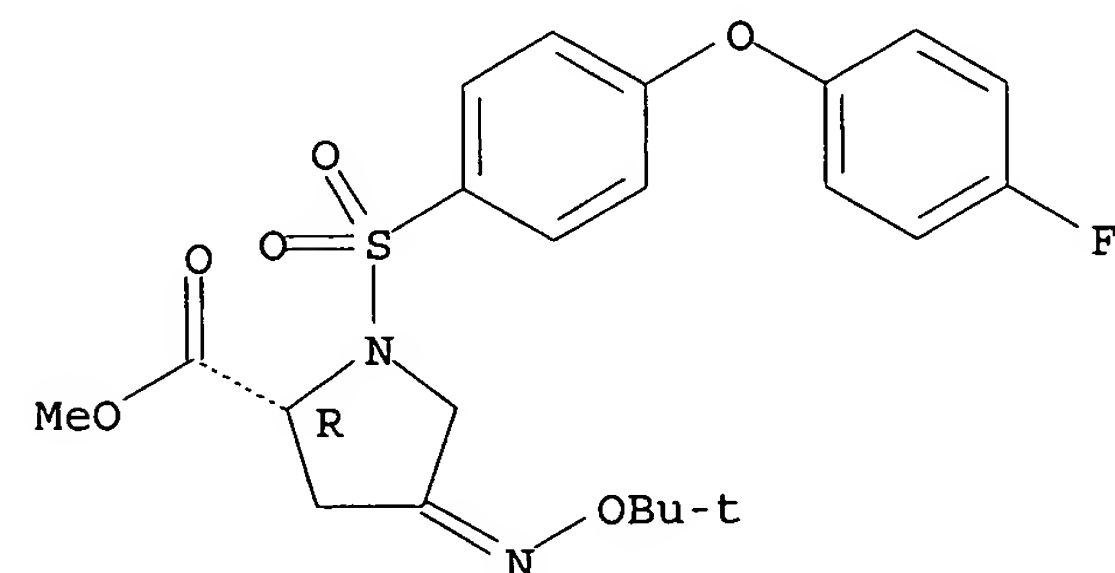
Absolute stereochemistry.  
Double bond geometry unknown.



RN 247058-79-3 HCAPLUS

CN D-Proline, 4-[(1,1-dimethylethoxy)imino]-1-[[4-(4-fluorophenoxy)phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



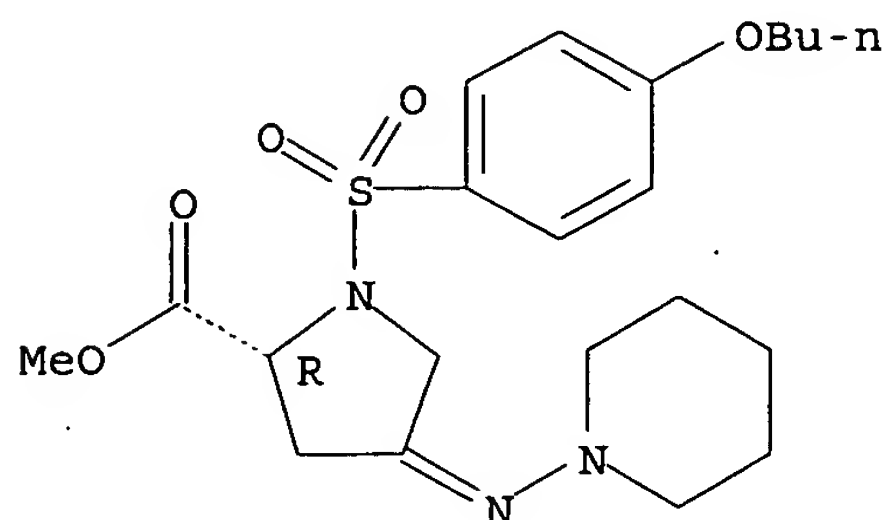
RN 247058-80-6 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(1-piperidinylimino)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



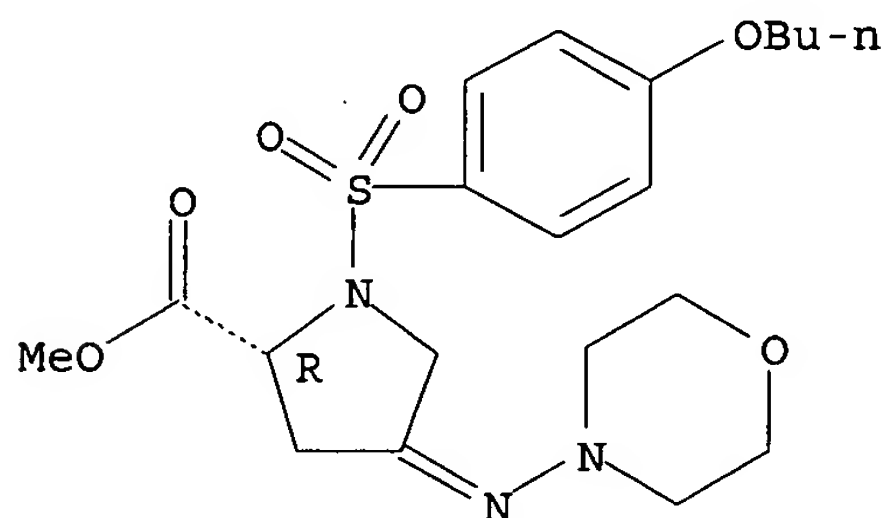
Double bond geometry unknown.



RN 247058-81-7 HCAPLUS

CN D-Proline, 1-[(4-butoxyphenyl)sulfonyl]-4-(4-morpholinylimino)-, methyl ester (9CI) (CA INDEX NAME)

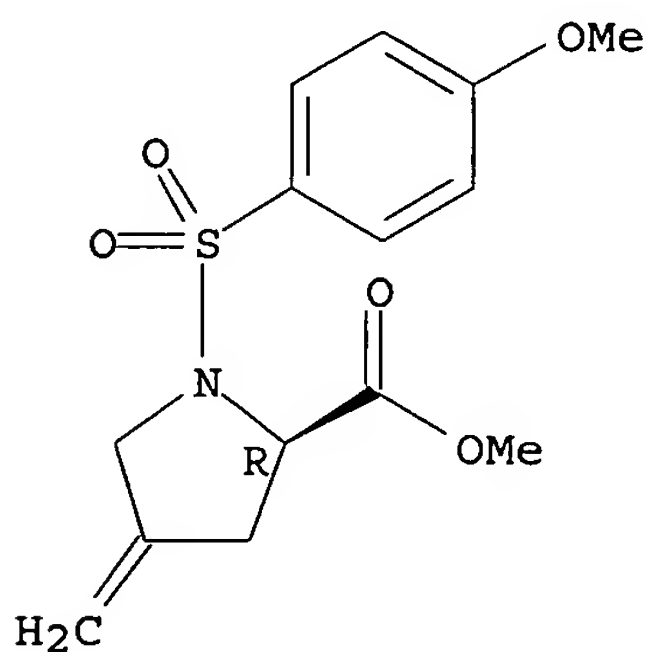
Absolute stereochemistry.  
Double bond geometry unknown.



RN 247058-82-8 HCAPLUS

CN D-Proline, 1-[(4-methoxyphenyl)sulfonyl]-4-methylene-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

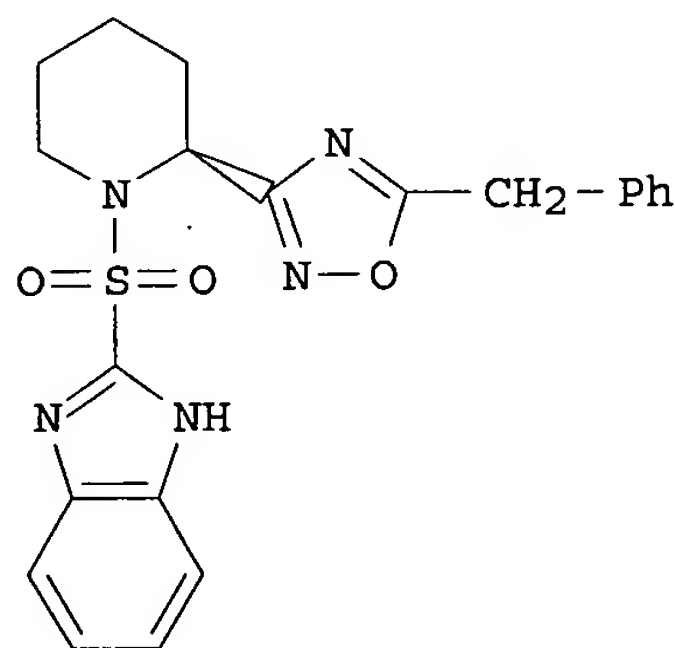
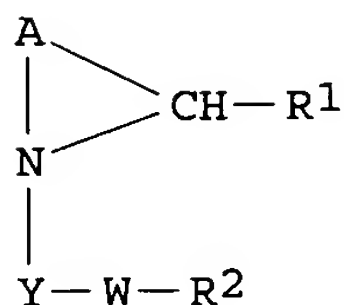
L32 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:576925 HCAPLUS

DOCUMENT NUMBER: 131:214289

TITLE: Preparation of oxadiazolyl piperidine derivatives as  
rotamase **enzyme inhibitors**  
INVENTOR(S): Bull, David John; MaGuire, Robert John; Palmer,  
Michael John; Wythes, Martin James  
PATENT ASSIGNEE(S): Pfizer Inc., USA; Pfizer Ltd.  
SOURCE: PCT Int. Appl., 237 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: **Patent**  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945006	A1	19990910	WO 1999-IB259	19990215 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2322442	AA	19990910	CA 1999-2322442	19990215 <--
AU 9921810	A1	19990920	AU 1999-21810	19990215 <--
BR 9908480	A	20001205	BR 1999-8480	19990215 <--
EP 1060178	A1	20001220	EP 1999-901847	19990215 <--
EP 1060178	B1	20030903		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002505329	T2	20020219	JP 2000-534548	19990215 <--
AT 248836	E	20030915	AT 1999-901847	19990215 <--
PT 1060178	T	20031231	PT 1999-901847	19990215
ES 2204101	T3	20040416	ES 1999-901847	19990215
US 6610707	B1	20030826	US 1999-380427	19990901 <--
PRIORITY APPLN. INFO.:			GB 1998-4426	A 19980302
			WO 1999-IB259	W 19990215
OTHER SOURCE(S):			MARPAT 131:214289	
GI				



AB Oxadiazolyl piperidine derivs. and analogs (I) [R1 = 5- or 6-membered heteroaryl (un)substituted ring containing 1-4 N, or 1 S or O and/or 1-2 N atoms; R2 = H, (un)substituted Ph, (un)substituted C3-7 cycloalkyl, or 5-, 6-, or 7-membered (un)substituted heterocycle; A = C3-5 alkylene; W =

direct link, C1-6 alkylene, or C2-6 alkenylene; X = direct link, C1-6 alkylene, or alkylene-Z-alkylene; Y = SO<sub>2</sub>, CO, (un)substituted CO-NH, CO-CO, CH<sub>2</sub>-CO, CS-CO, CO-CS, or CO-CH(OH); Z = O, S, (un)substituted CH<sub>2</sub>-NH, CH(aryl), NH, NH-CO<sub>2</sub>, CO-NH, or NH-CO] were prepared as rotamase **enzyme inhibitors**, particularly FKBP-12 and FKBP-52

**inhibitors**, to moderate neuronal regeneration and outgrowth.

Thus, ethyldiisopropylamine was added to a mixture of 5-benzyl-3-[(2S)-2-piperidyl]-1,2,4-oxadiazole hydrochloride (preparation given) and 1H-benzo[d]imidazole-2-sulfonyl chloride (preparation given) in CH<sub>2</sub>Cl<sub>2</sub> and the mixture was stirred for 18 h to yield 1H-benzo[d]imidazol-2-yl [(2S)-2-(5-benzyl-1,2,4-oxadiazol-3-yl)-1-piperidyl] sulfone (II). Seven compds. of the invention were tested for in vitro **inhibitory** activity against the FKBP-12 **enzyme** in a coupled colorimetric PPlase assay, and exhibited IC<sub>50</sub> values in the range of 81 nm to 2010 nm. One compound was assayed for **inhibitory** activity against the FKBP-52 **enzyme** and gave a K<sub>i</sub> value of 685. The compds. are claimed to be useful in treating neurol. disorders arising from neurodegenerative diseases and nerve damage.

IT 242459-55-8P 242459-66-1P 242459-72-9P

242459-74-1P 242459-78-5P 242459-94-5P

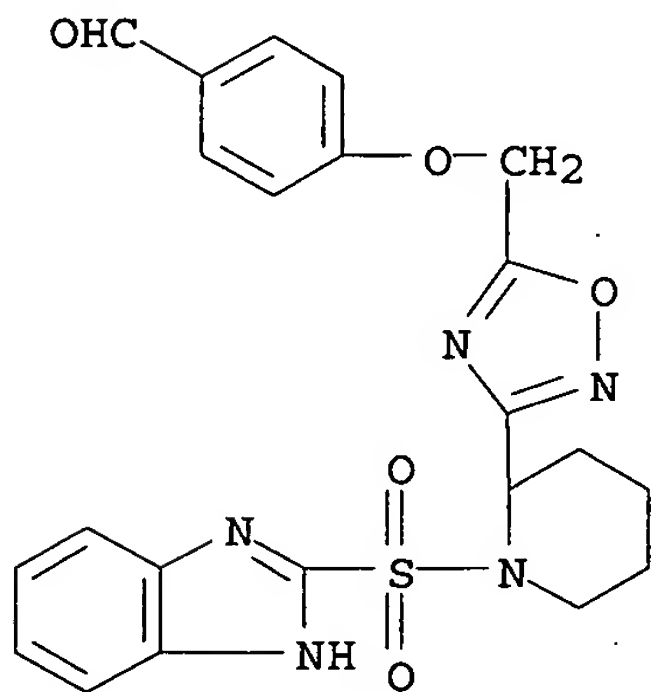
242459-95-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of oxadiazolyl piperidine derivs. as rotamase **enzyme inhibitors** for treatment of neurol. disorders arising from neurodegenerative diseases and nerve damage)

RN 242459-55-8 HCAPLUS

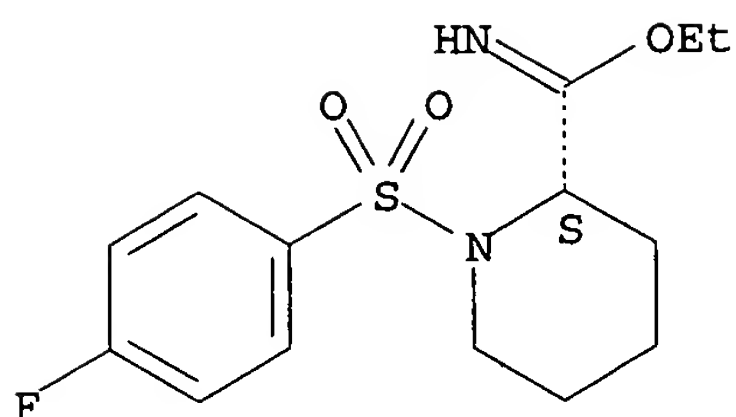
CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[(4-formylphenoxy)methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



RN 242459-66-1 HCAPLUS

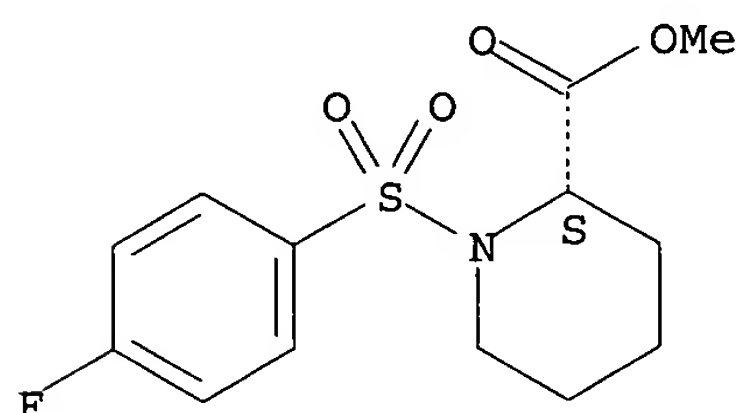
CN 2-Piperidinecarboximidic acid, 1-[(4-fluorophenyl)sulfonyl]-, ethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



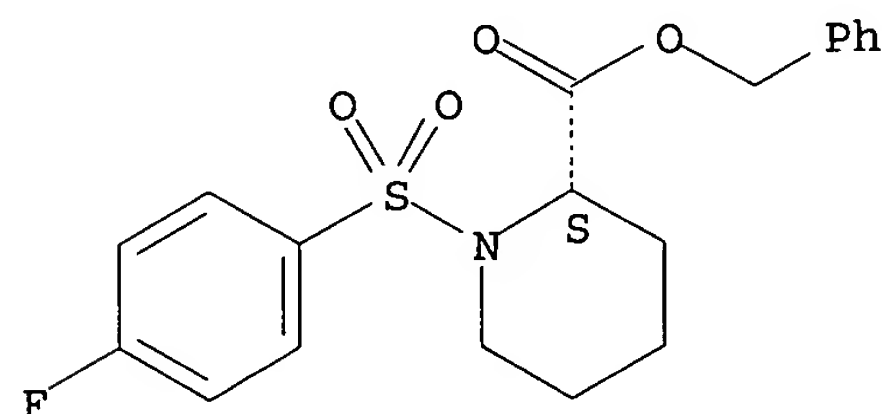
RN 242459-72-9 HCAPLUS  
 CN 2-Piperidinecarboxylic acid, 1-[(4-fluorophenyl)sulfonyl]-, methyl ester,  
 (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

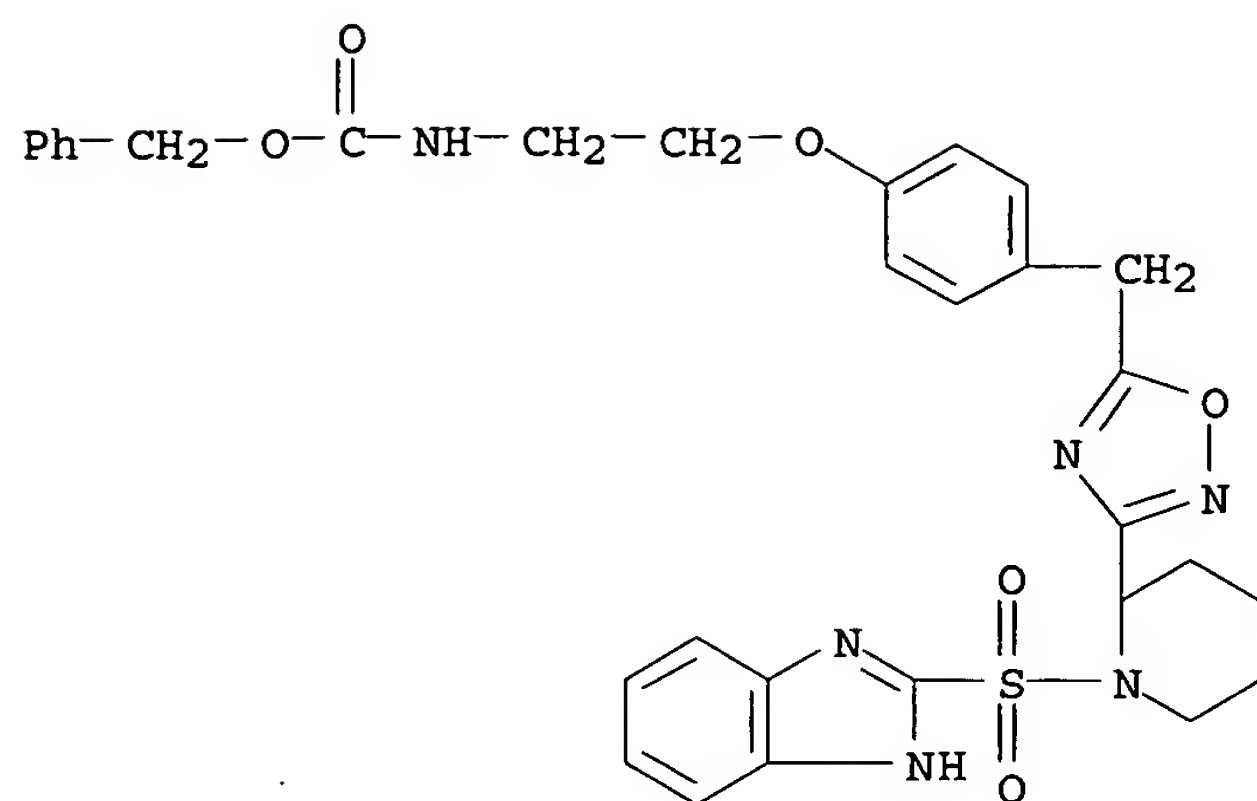


RN 242459-74-1 HCAPLUS  
 CN 2-Piperidinecarboxylic acid, 1-[(4-fluorophenyl)sulfonyl]-, phenylmethyl  
 ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



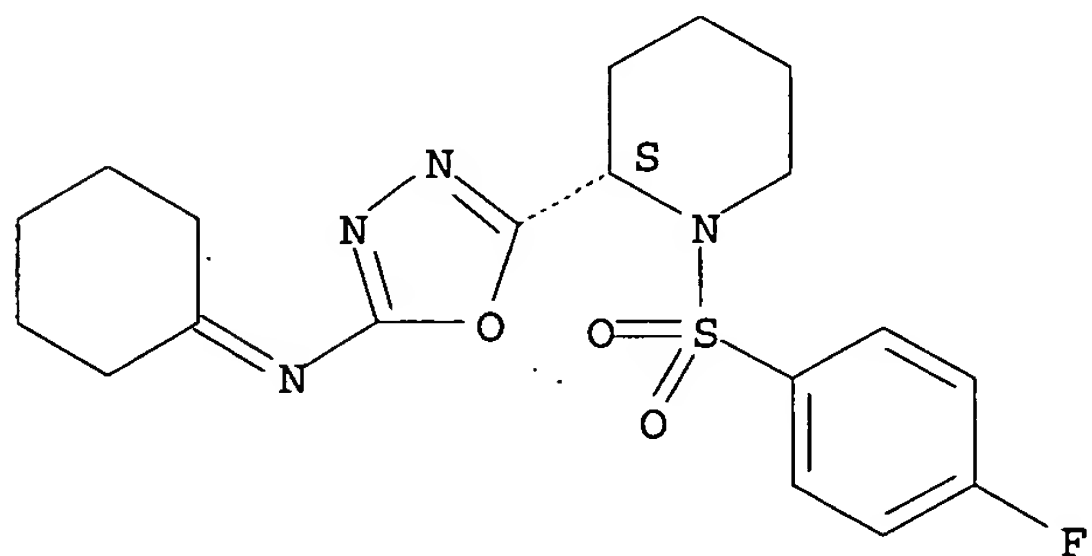
RN 242459-78-5 HCAPLUS  
 CN Carbamic acid, [2-[4-[[3-[1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-  
 1,2,4-oxadiazol-5-yl]methyl]phenoxy]ethyl]-, phenylmethyl ester (9CI) (CA  
 INDEX NAME)



RN 242459-94-5 HCAPLUS

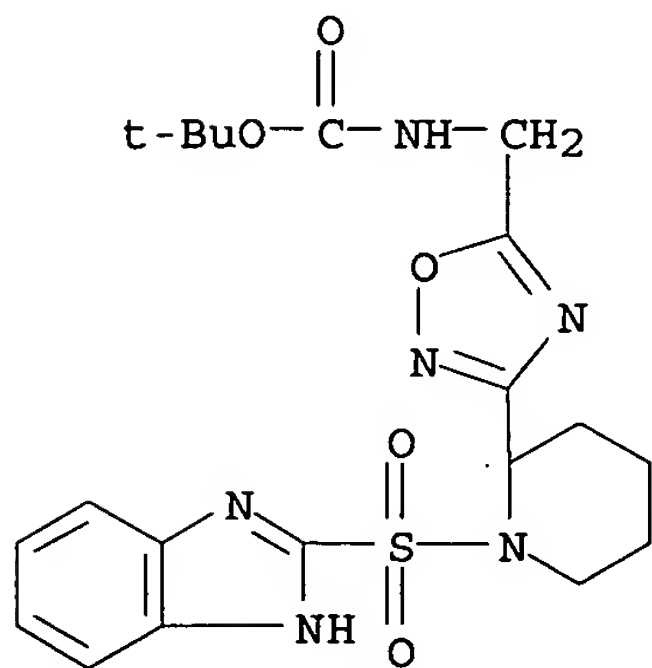
CN Piperidine, 2-[5-(cyclohexylideneamino)-1,3,4-oxadiazol-2-yl]-1-[(4-fluorophenyl)sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 242459-95-6 HCAPLUS

CN Carbamic acid, [[3-[1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-1,2,4-oxadiazol-5-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 242458-82-8P 242458-83-9P 242458-98-6P  
 242458-99-7P 242459-04-7P 242459-24-1P  
 242459-27-4P 242459-38-7P 242459-40-1P

242459-41-2P 242459-42-3P 242459-43-4P

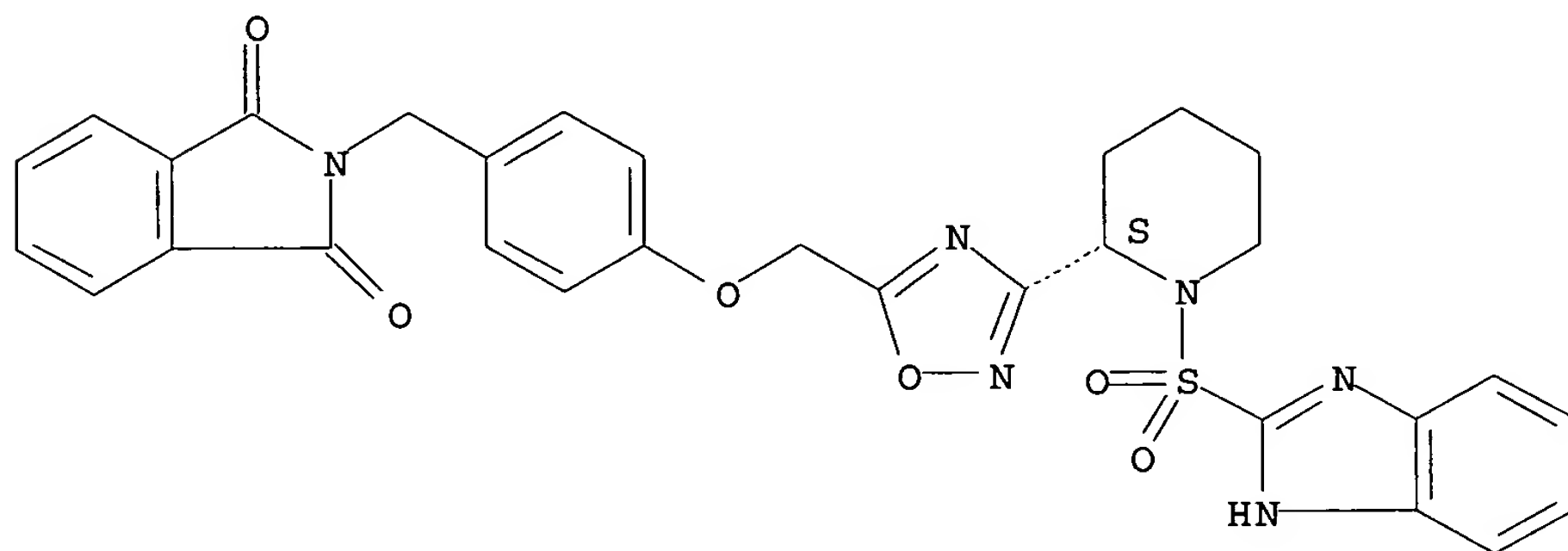
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of oxadiazolyl piperidine derivs. as rotamase **enzyme inhibitors** for treatment of neurol. disorders arising from neurodegenerative diseases and nerve damage)

RN 242458-82-8 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

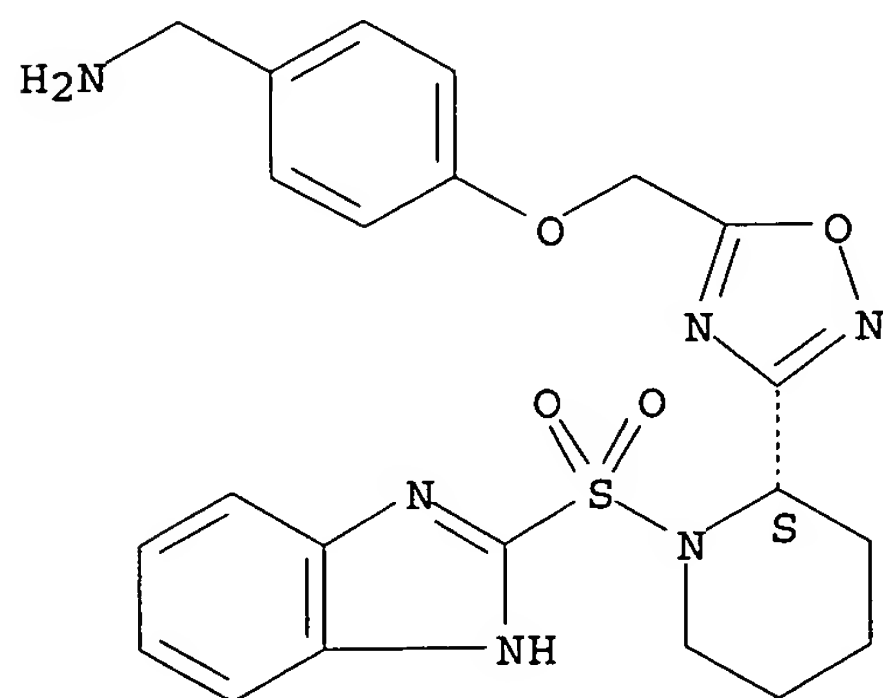
Absolute stereochemistry. Rotation (-).



RN 242458-83-9 HCAPLUS

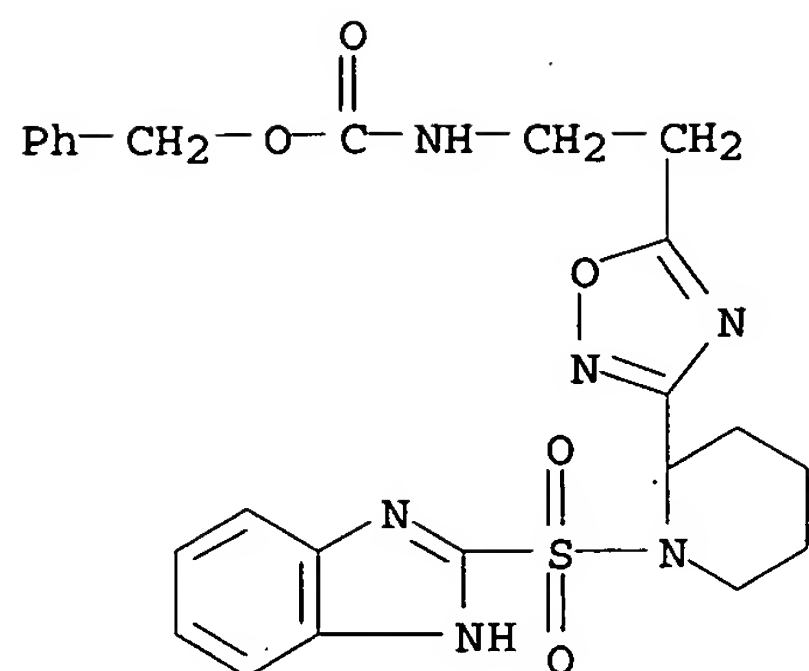
CN Piperidine, 2-[5-[[4-(aminomethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-1-(1H-benzimidazol-2-ylsulfonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

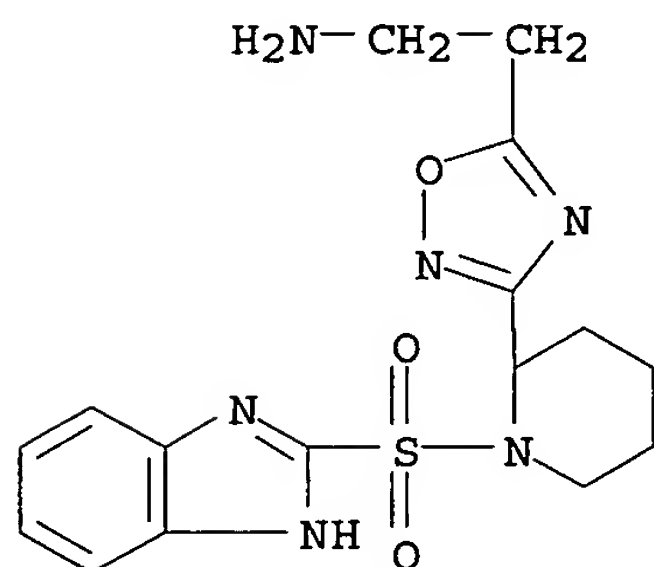


RN 242458-98-6 HCAPLUS

CN Carbamic acid, [2-[3-[1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-1,2,4-oxadiazol-5-yl]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

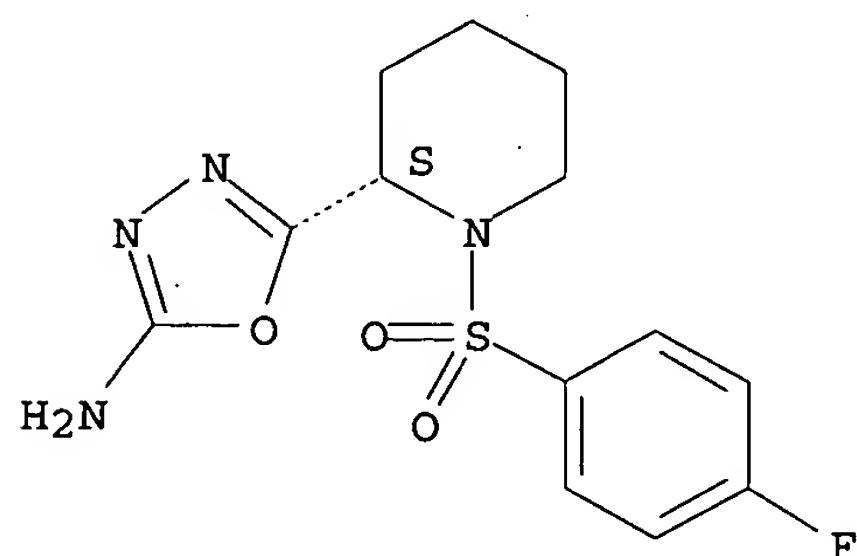


RN 242458-99-7 HCAPLUS  
 CN Piperidine, 2-[5-(2-aminoethyl)-1,2,4-oxadiazol-3-yl]-1-(1H-benzimidazol-2-ylsulfonyl)- (9CI) (CA INDEX NAME)



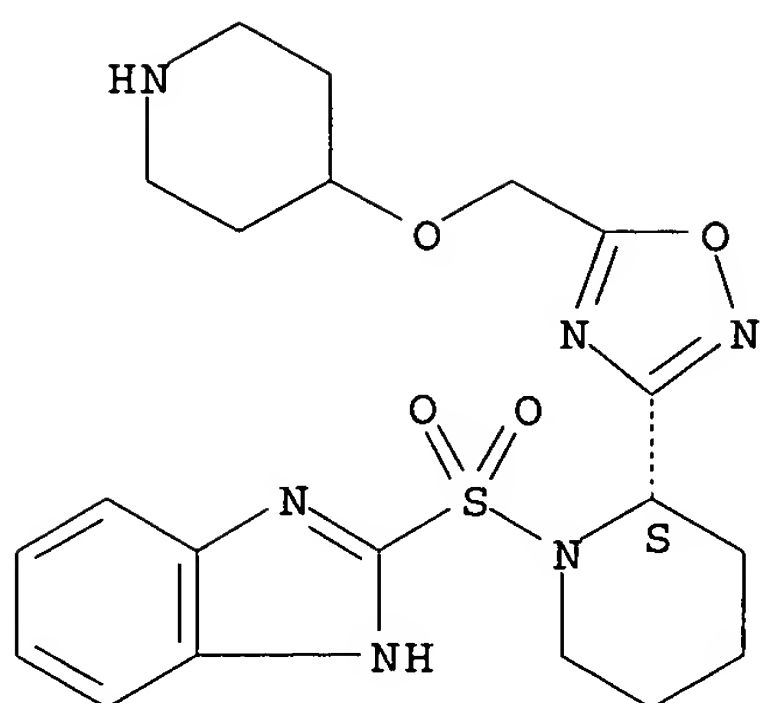
RN 242459-04-7 HCAPLUS  
 CN Piperidine, 2-(5-amino-1,3,4-oxadiazol-2-yl)-1-[(4-fluorophenyl)sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 242459-24-1 HCAPLUS  
 CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[(4-piperidinyloxy)methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

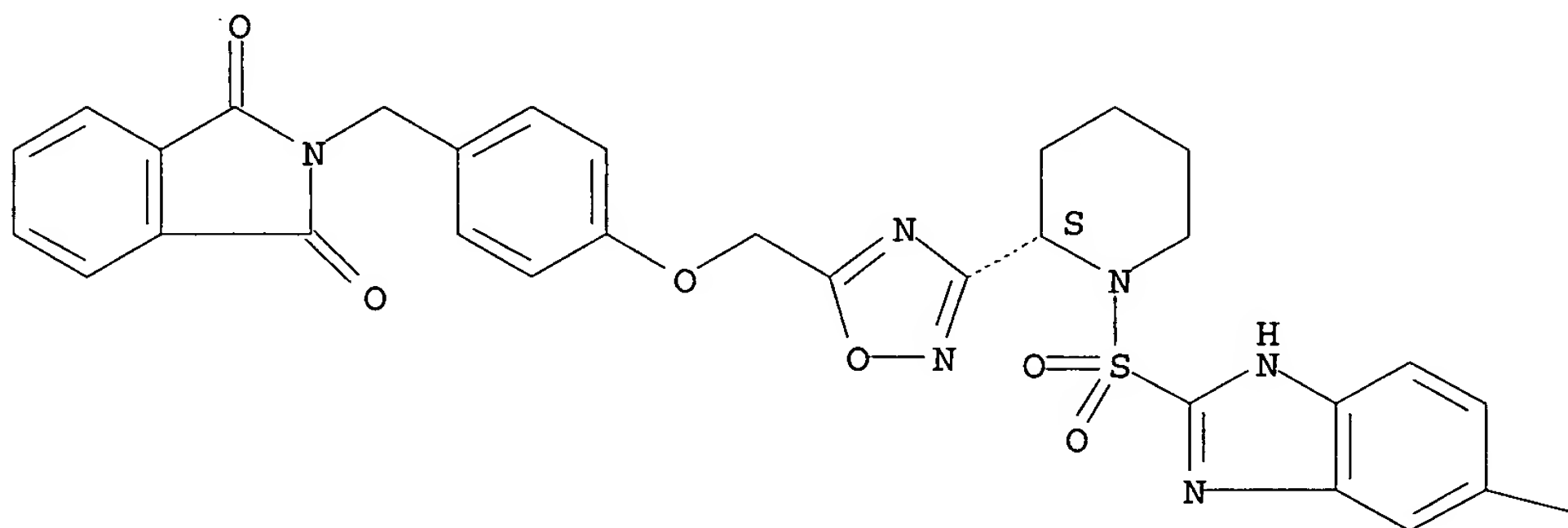


RN 242459-27-4 HCAPLUS

CN Piperidine, 1-[(5-bromo-1H-benzimidazol-2-yl)sulfonyl]-2-[5-[[4-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

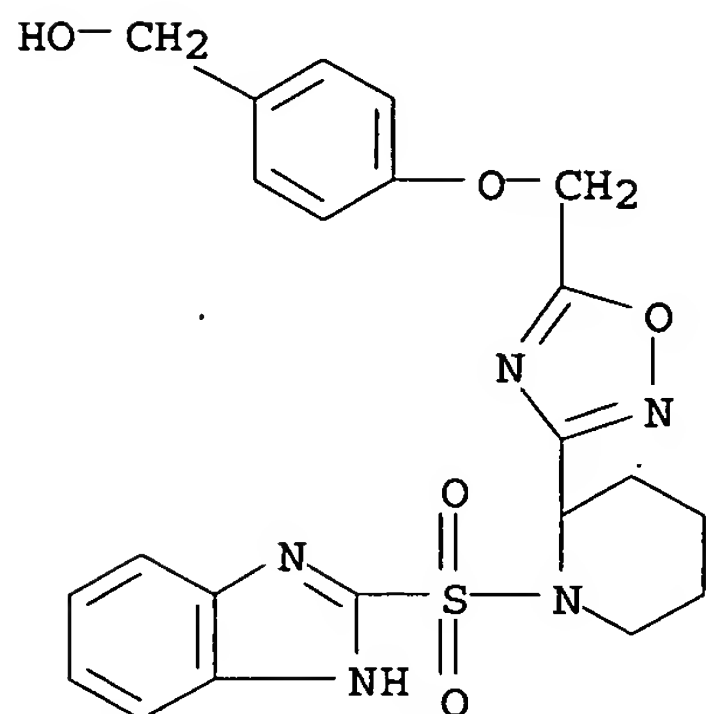
Br

RN 242459-38-7 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-



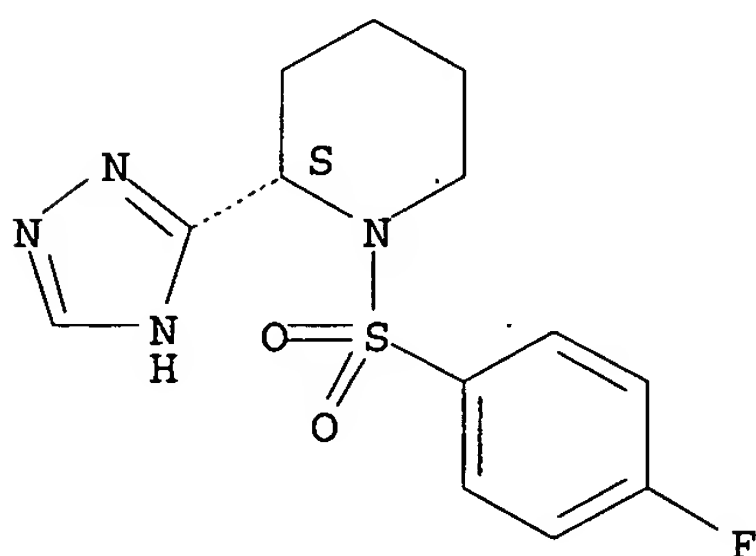
(hydroxymethyl)phenoxy)methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



RN 242459-40-1 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(1H-1,2,4-triazol-3-yl)-, (2S)- (9CI) (CA INDEX NAME)

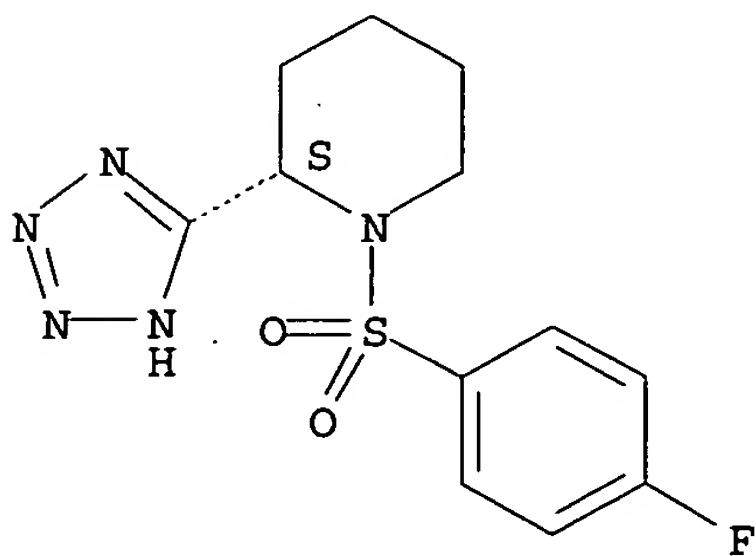
Absolute stereochemistry.



RN 242459-41-2 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(1H-tetrazol-5-yl)-, (2S)- (9CI) (CA INDEX NAME)

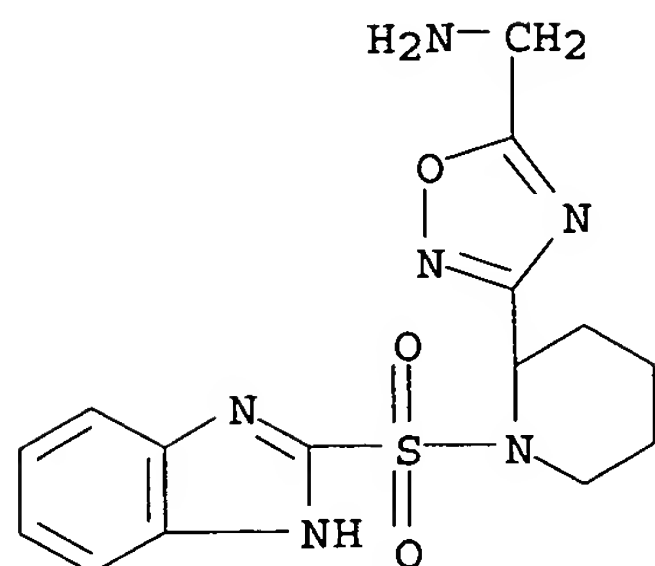
Absolute stereochemistry. Rotation (-).



RN 242459-42-3 HCAPLUS

CN Piperidine, 2-[5-(aminomethyl)-1,2,4-oxadiazol-3-yl]-1-(1H-benzimidazol-2-

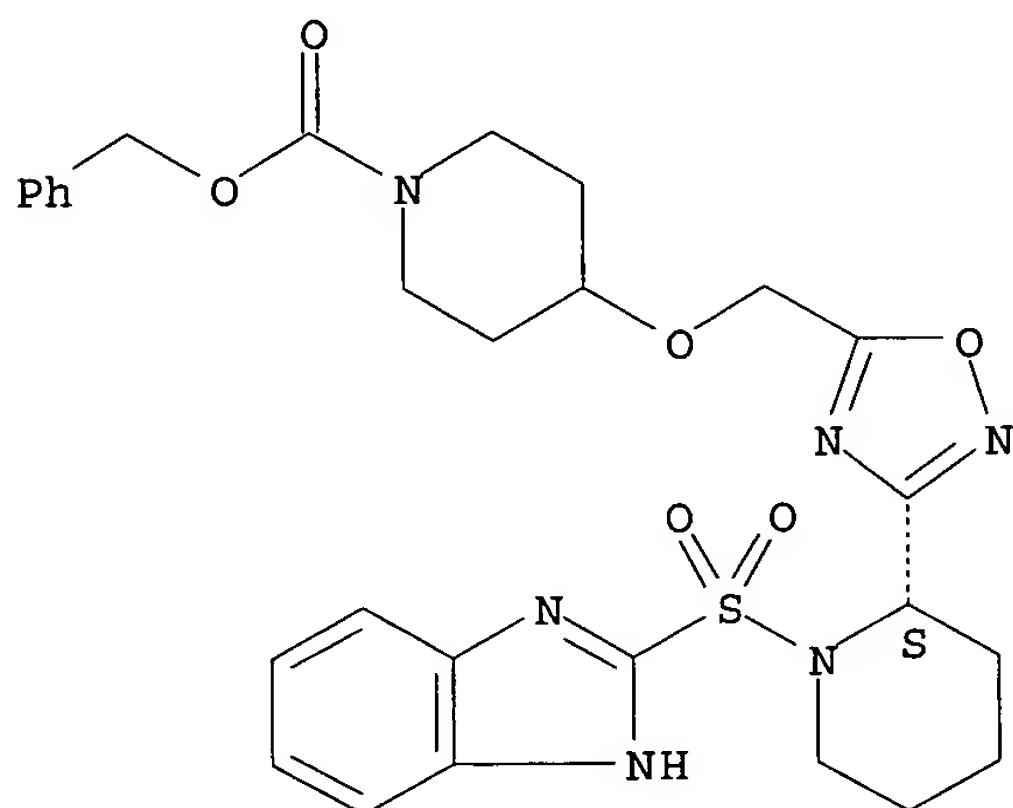
ylsulfonyl)- (9CI) (CA INDEX NAME)



RN 242459-43-4 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[3-[(2S)-1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyll-1,2,4-oxadiazol-5-yl]methoxy]-, phenylmethyl ester (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



IT 242458-73-7P 242458-74-8P 242458-84-0P  
242458-85-1P 242458-86-2P 242459-00-3P  
242459-01-4P 242459-02-5P 242459-03-6P  
242459-05-8P 242459-06-9P 242459-07-0P  
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242459-28-5P 242459-37-6P

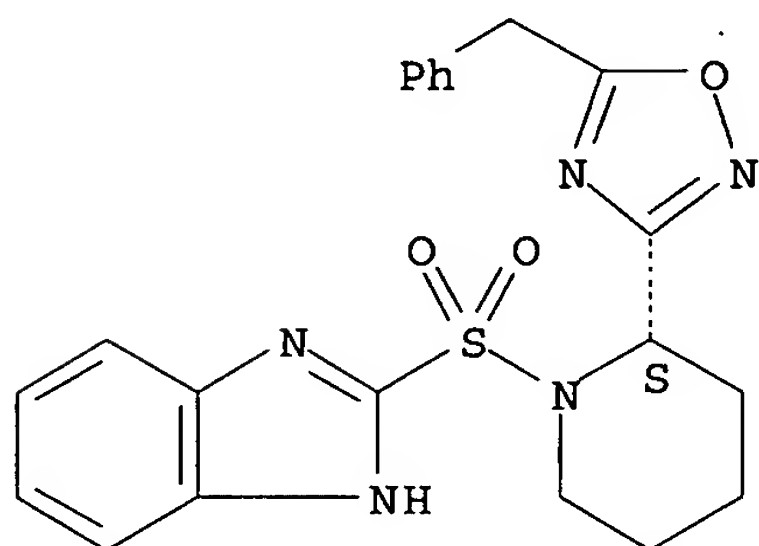
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of oxadiazolyl piperidine derivs. as rotamase **enzyme inhibitors** for treatment of neurol. disorders arising from neurodegenerative diseases and nerve damage)

RN 242458-73-7 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-(phenylmethyl)-1,2,4-

oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

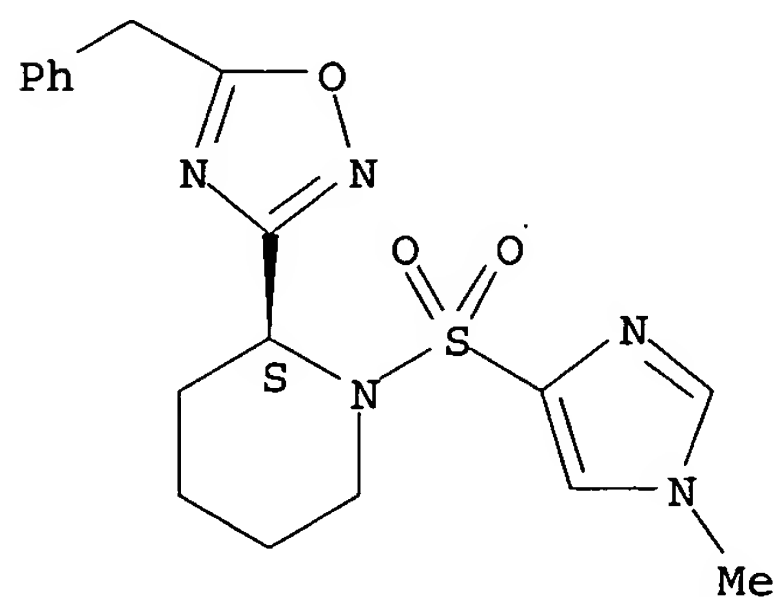
Absolute stereochemistry. Rotation (-).



RN 242458-74-8 HCAPLUS

CN Piperidine, 1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-2-[5-(phenylmethyl)-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

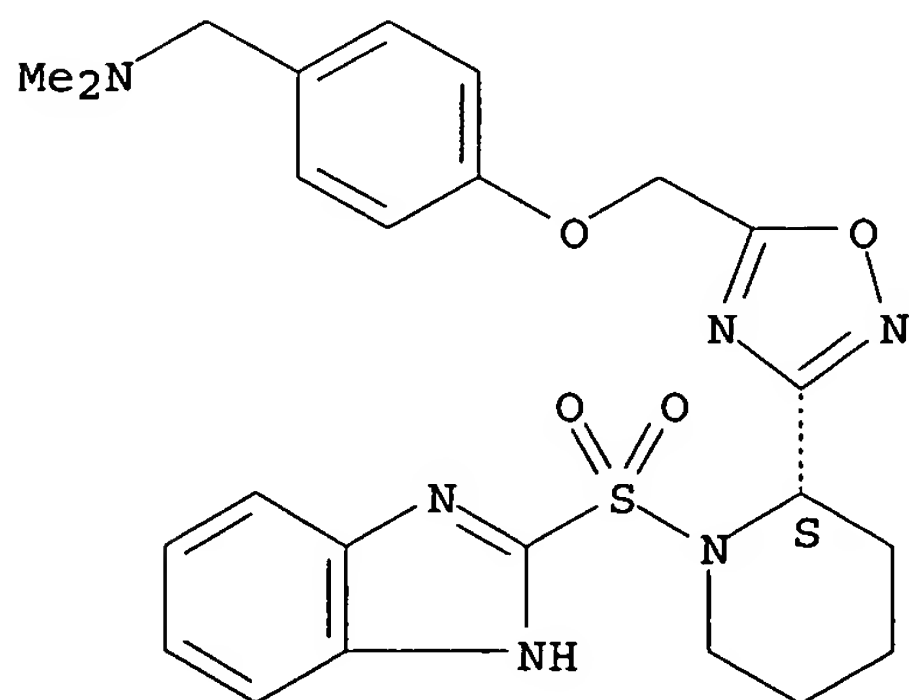
Absolute stereochemistry.



RN 242458-84-0 HCAPLUS

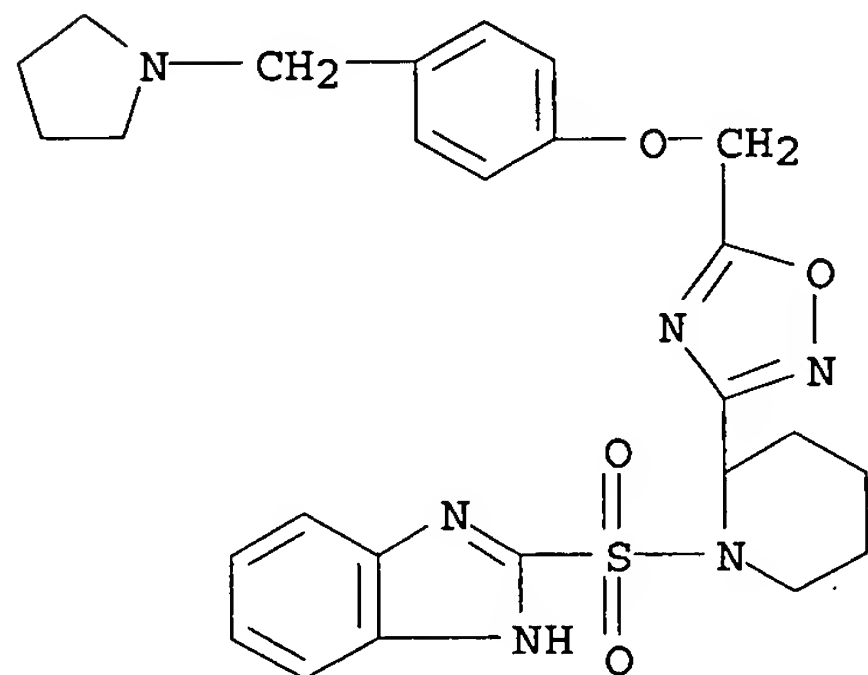
CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-[(dimethylamino)methyl]phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



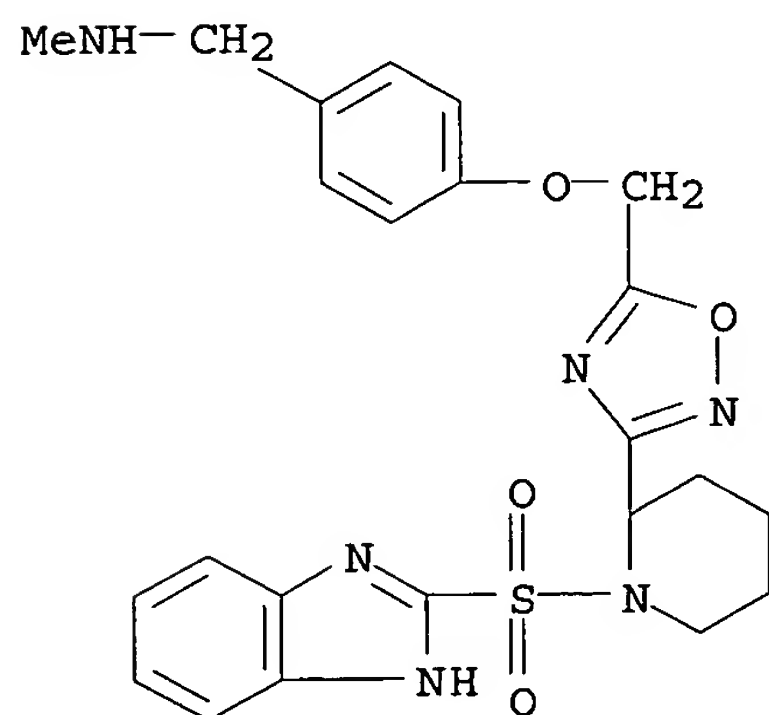
RN 242458-85-1 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-(1-pyrrolidinylmethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



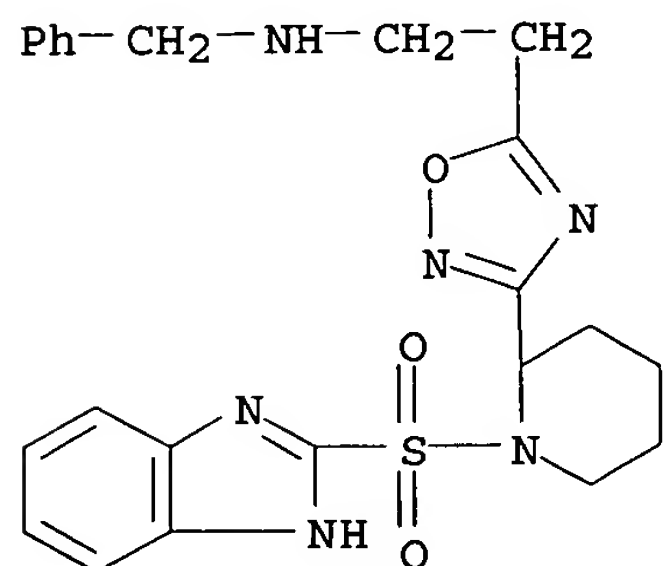
RN 242458-86-2 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[4-[(methylamino)methyl]phenoxy]methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



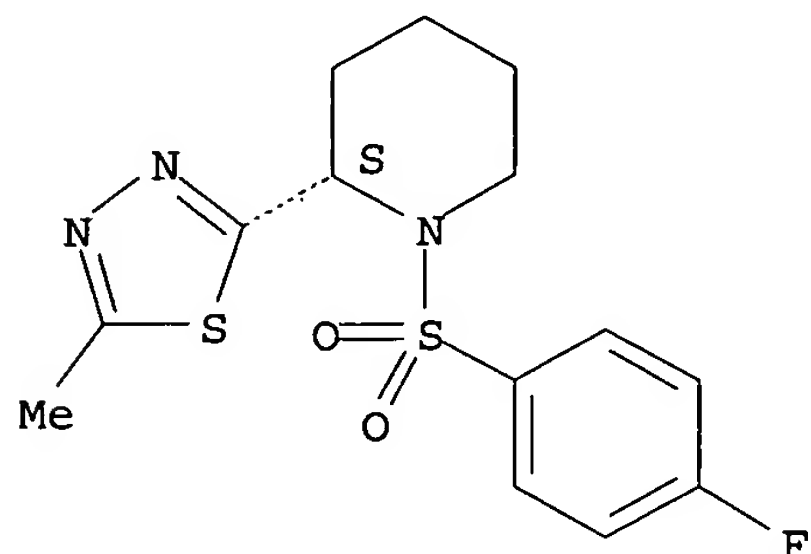
RN 242459-00-3 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[2-(phenylmethyl)amino]ethyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



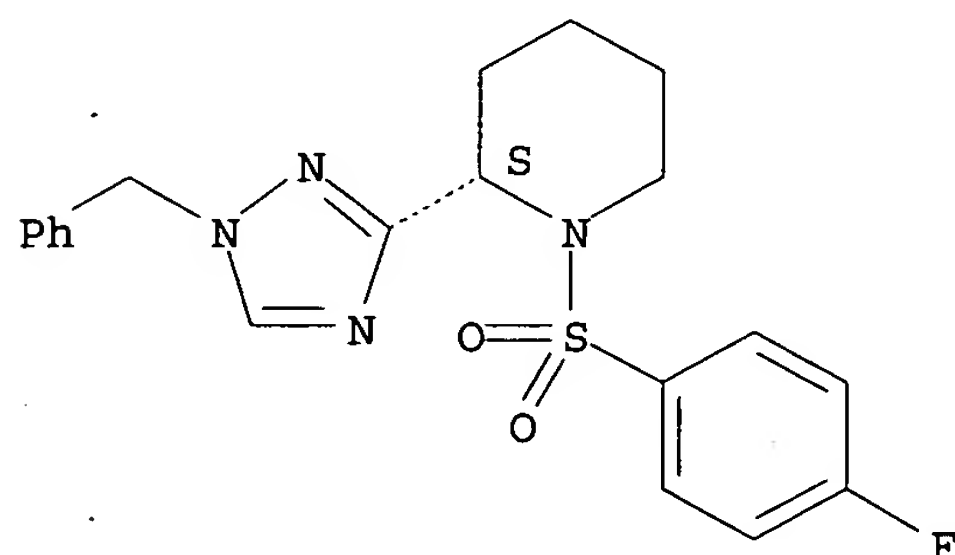
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 CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-methyl-1,3,4-thiadiazol-2-yl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



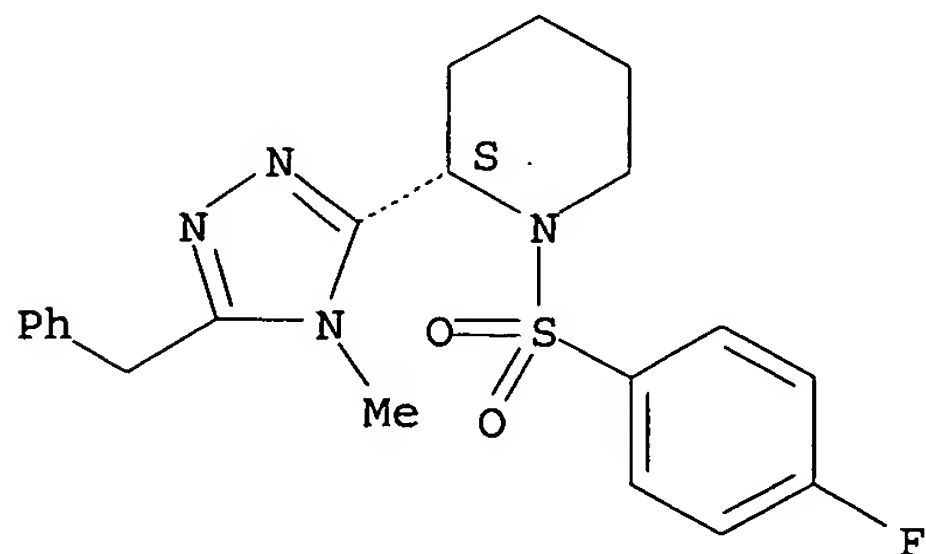
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Absolute stereochemistry.



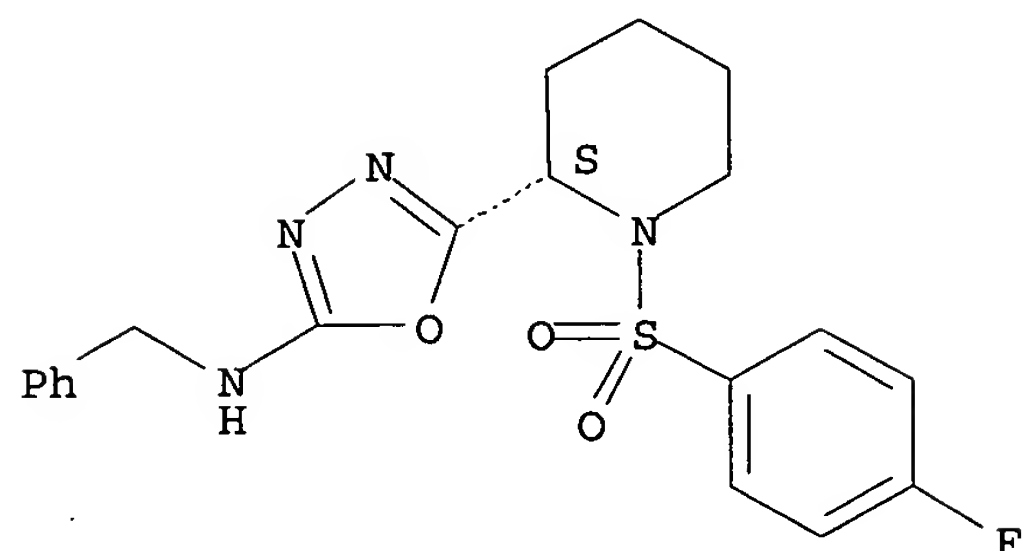
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Absolute stereochemistry. Rotation (-).



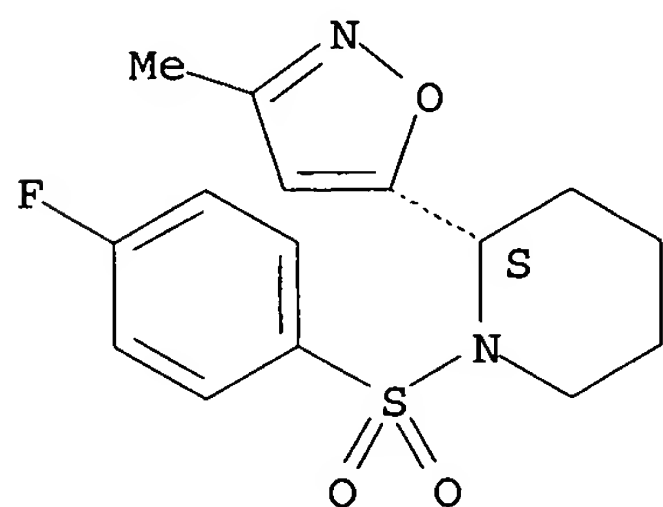
RN 242459-05-8 HCAPLUS  
 CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-[(phenylmethyl)amino]-1,3,4-oxadiazol-2-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



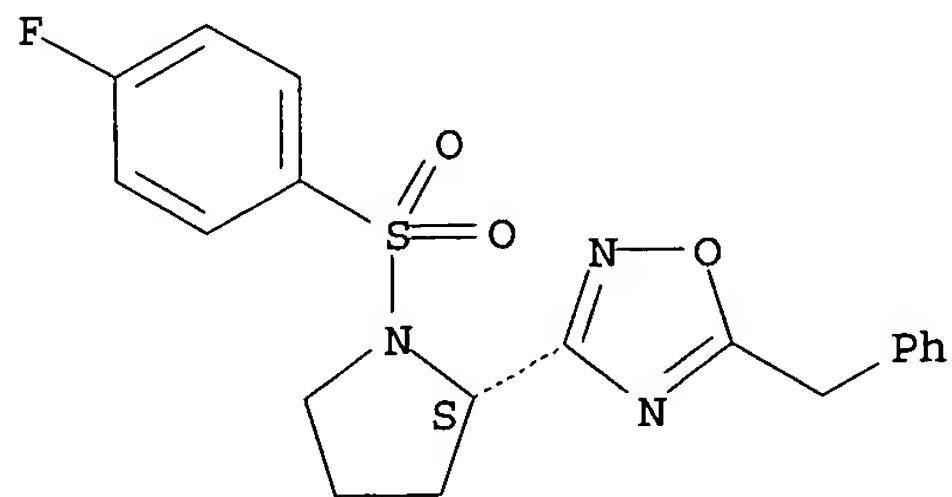
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CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(3-methyl-5-isoxazolyl)-, (2S)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



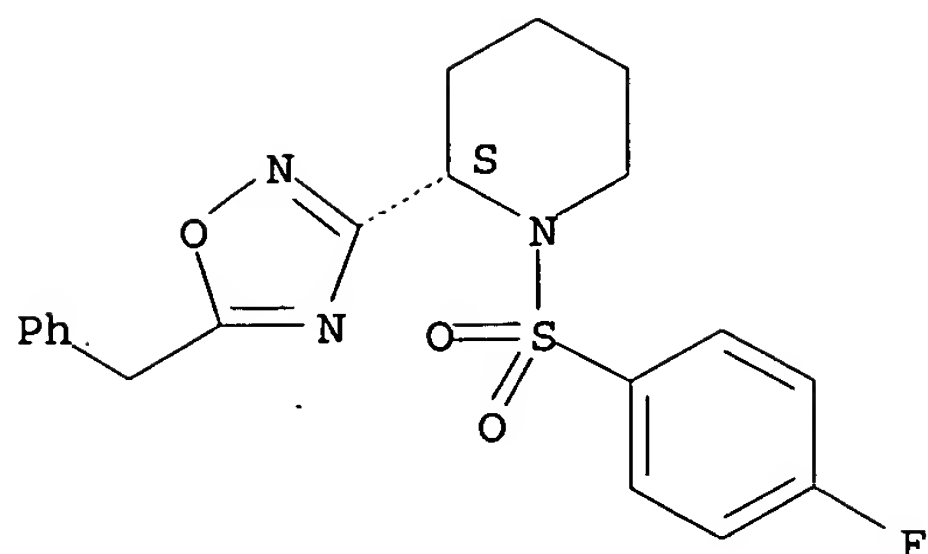
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CN Pyrrolidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-(phenylmethyl)-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



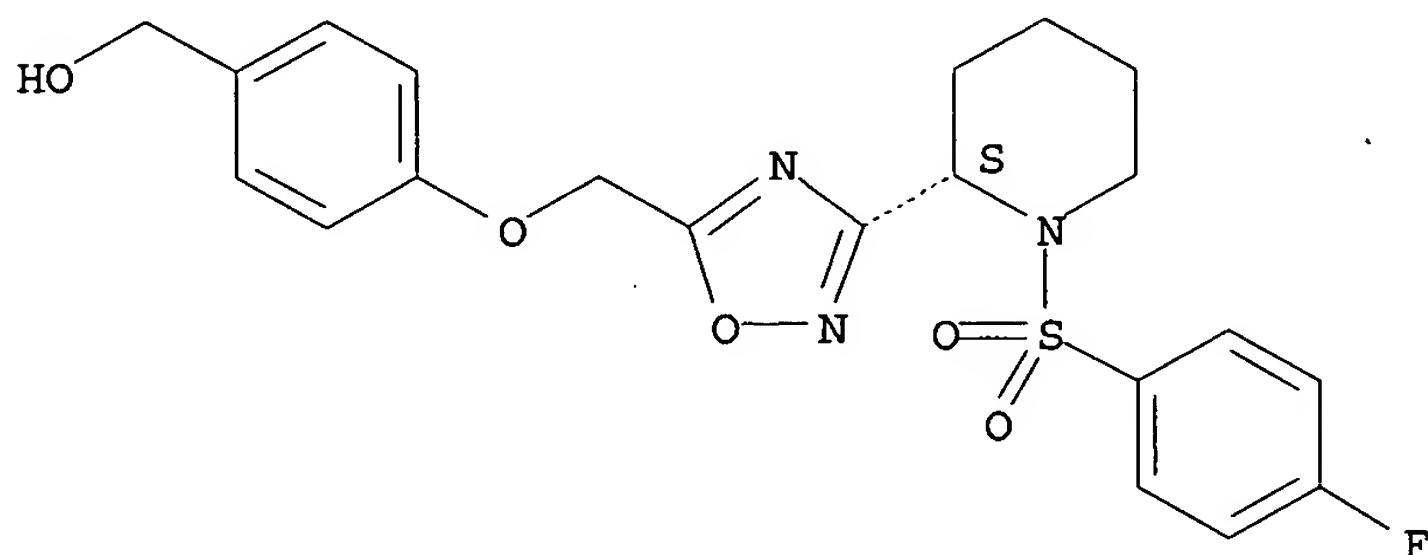
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CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-(phenylmethyl)-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



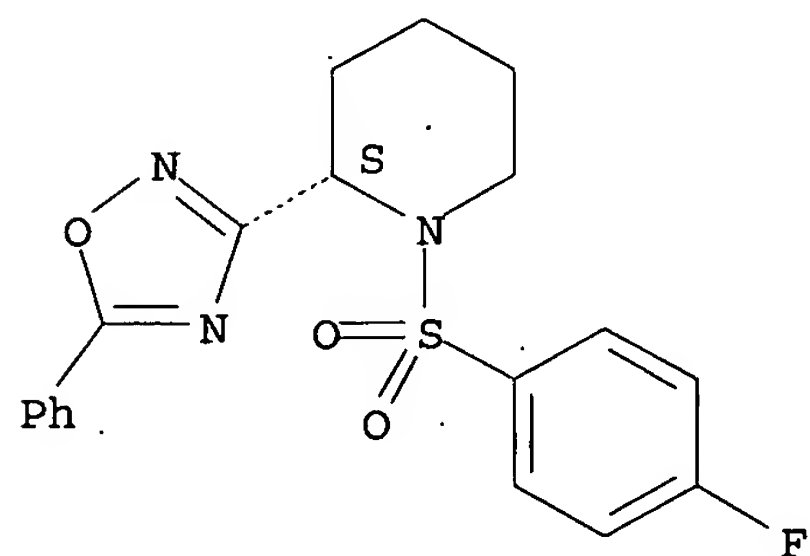
RN 242459-09-2 HCAPLUS  
 CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-[[4-(hydroxymethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



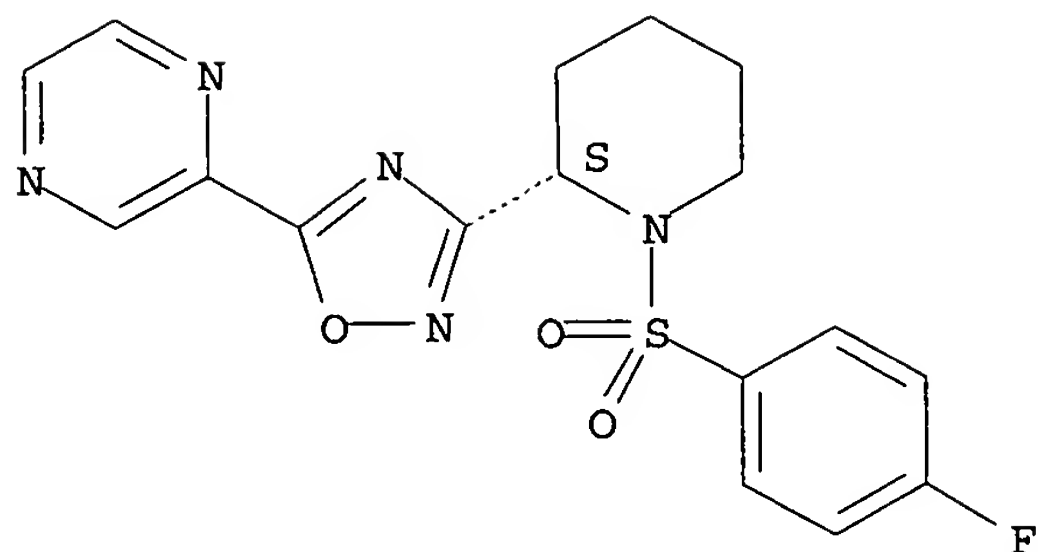
RN 242459-10-5 HCAPLUS  
 CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-phenyl-1,2,4-oxadiazol-3-yl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 242459-11-6 HCAPLUS  
 CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-pyrazinyl-1,2,4-oxadiazol-3-yl)-, (2S)- (9CI) (CA INDEX NAME)

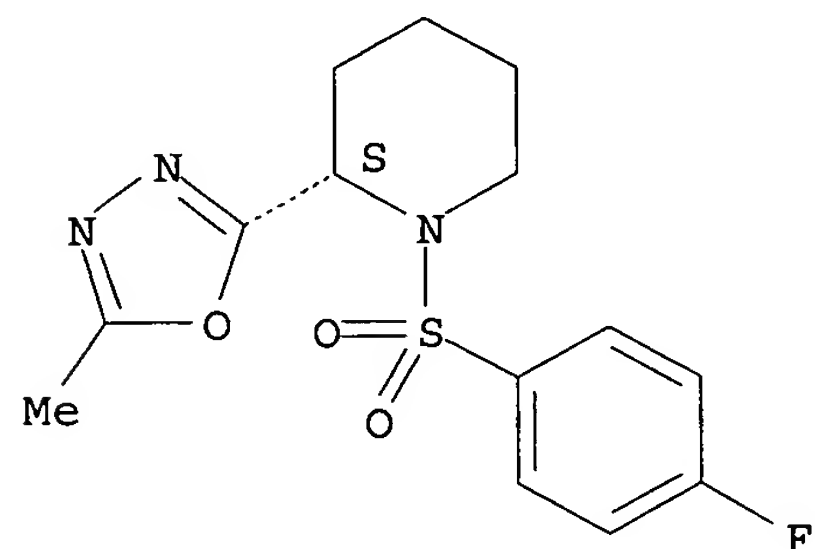
Absolute stereochemistry. Rotation (-).



RN 242459-12-7 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-methyl-1,3,4-oxadiazol-2-yl)-, (2S)- (9CI) (CA INDEX NAME)

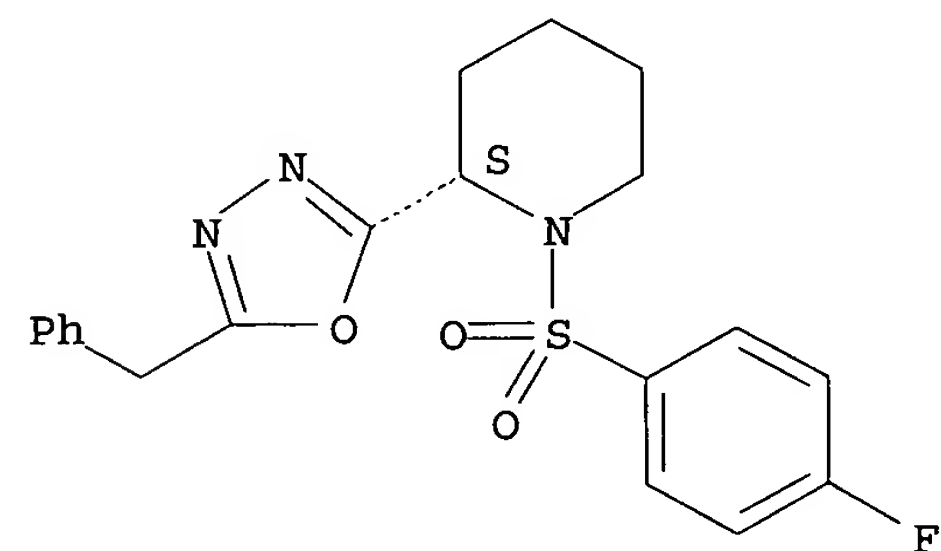
Absolute stereochemistry. Rotation (-).



RN 242459-13-8 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-(phenylmethyl)-1,3,4-oxadiazol-2-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

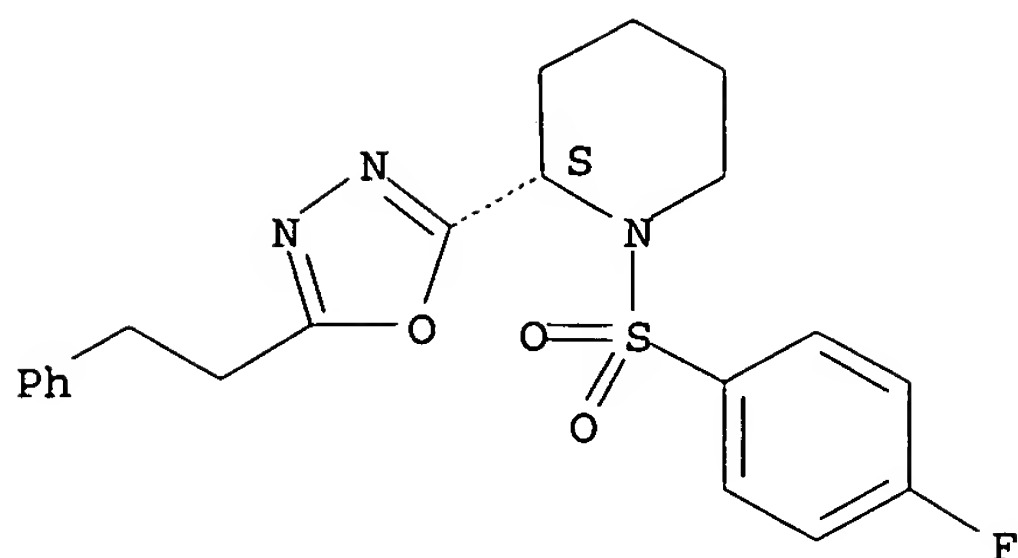


RN 242459-14-9 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[5-(2-phenylethyl)-1,3,4-oxadiazol-2-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

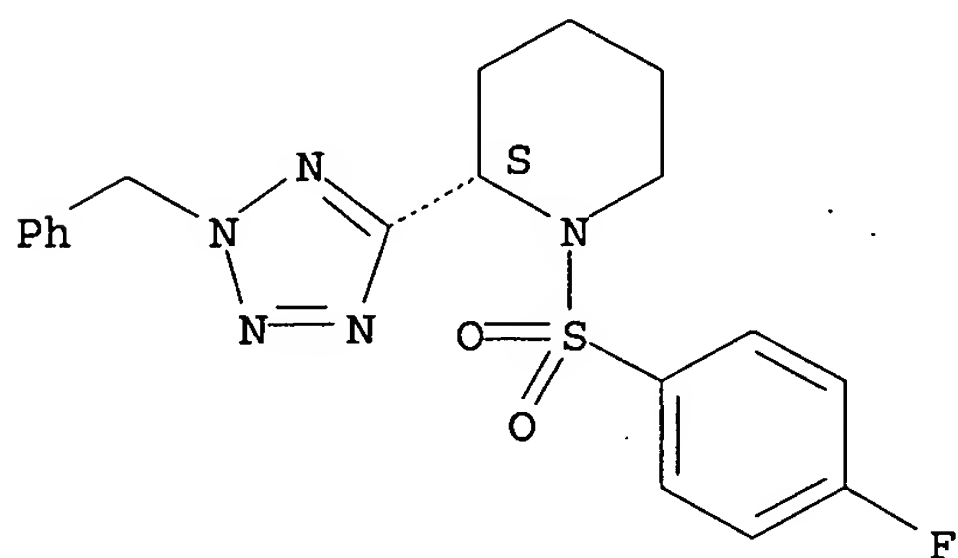




RN 242459-15-0 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-[2-(phenylmethyl)-2H-tetrazol-5-yl]-, (2S)- (9CI) (CA INDEX NAME)

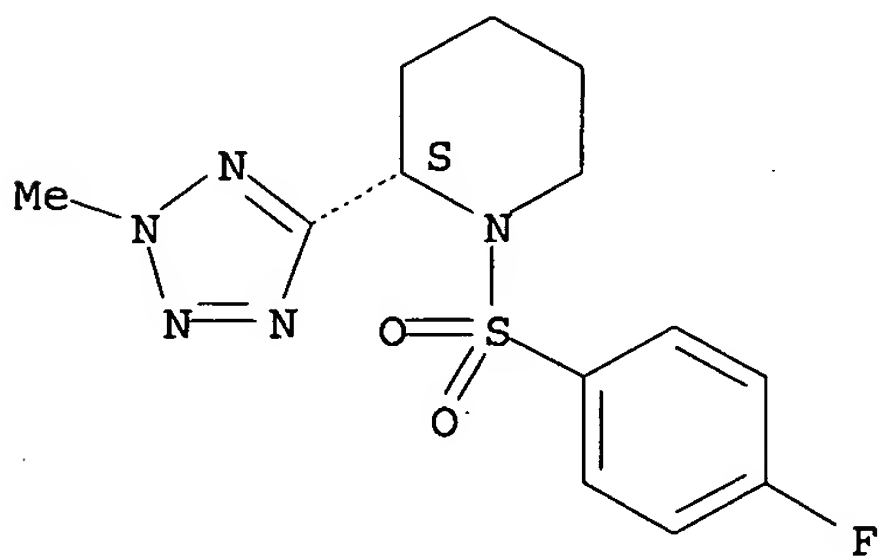
Absolute stereochemistry. Rotation (-).



RN 242459-16-1 HCAPLUS

CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(2-methyl-2H-tetrazol-5-yl)-, (2S)- (9CI) (CA INDEX NAME)

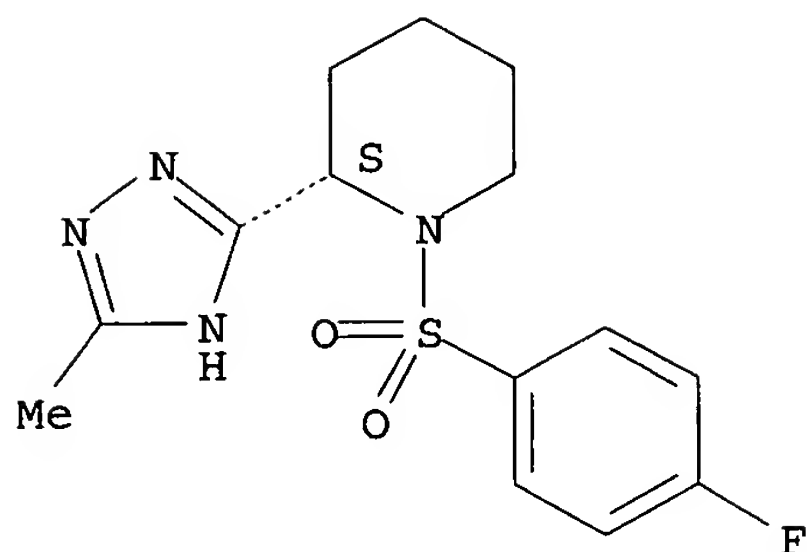
Absolute stereochemistry. Rotation (-).



RN 242459-17-2 HCAPLUS

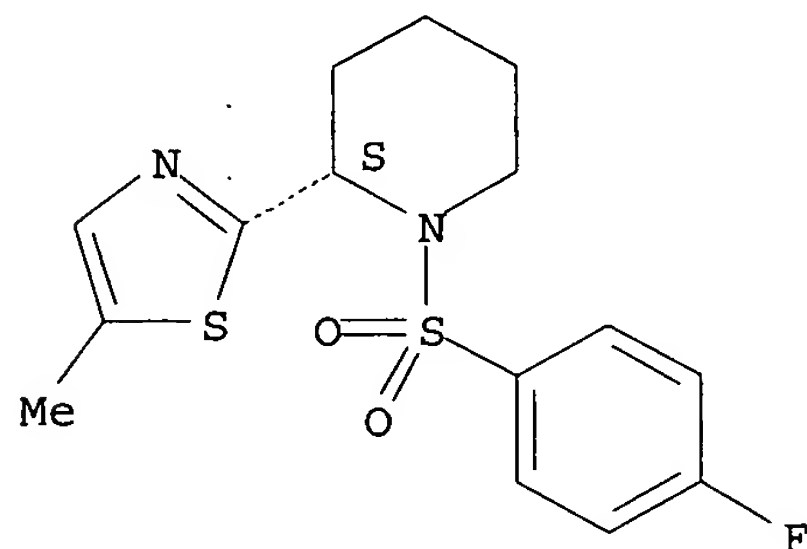
CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-methyl-1H-1,2,4-triazol-3-yl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



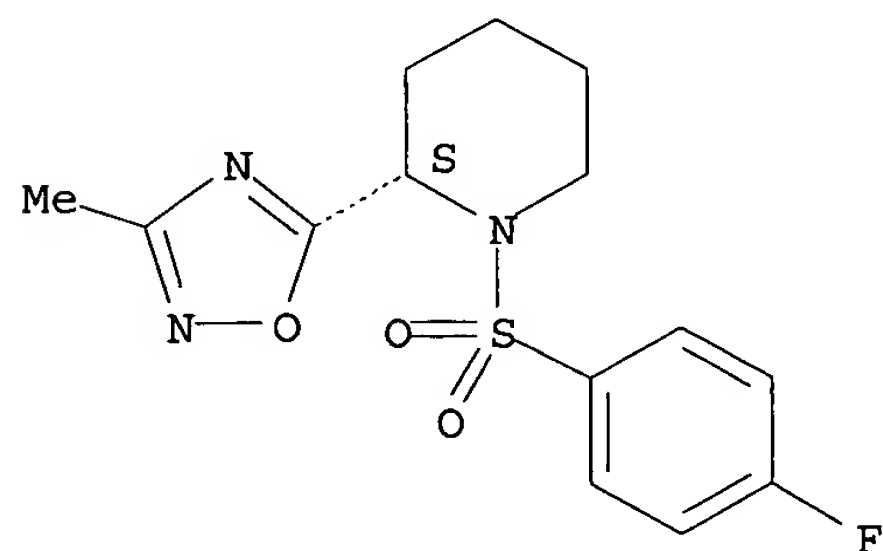
RN 242459-18-3 HCAPLUS  
 CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(5-methyl-2-thiazolyl)-, (2S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



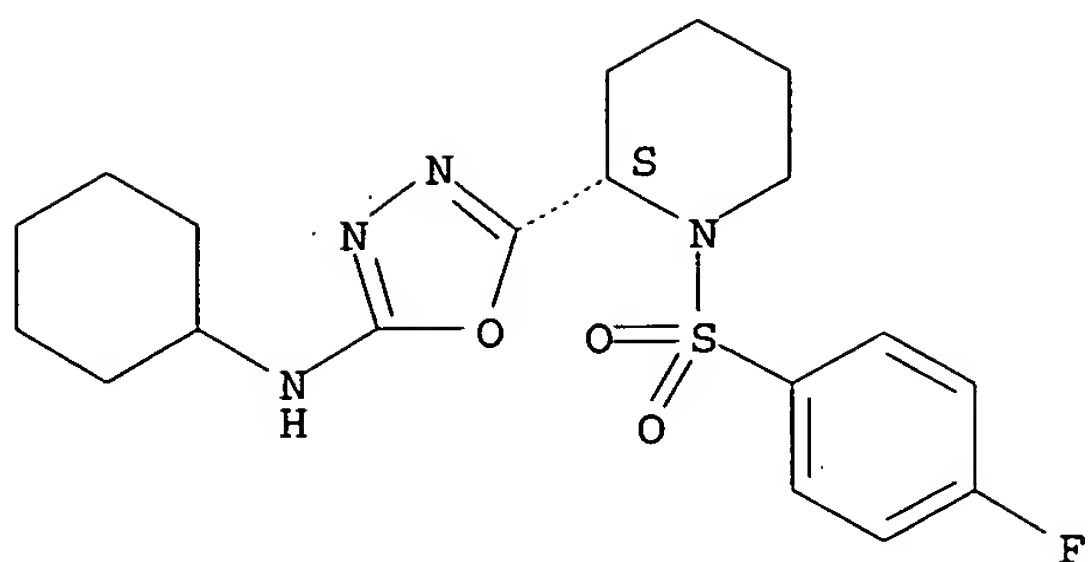
RN 242459-19-4 HCAPLUS  
 CN Piperidine, 1-[(4-fluorophenyl)sulfonyl]-2-(3-methyl-1,2,4-oxadiazol-5-yl)-  
 , (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



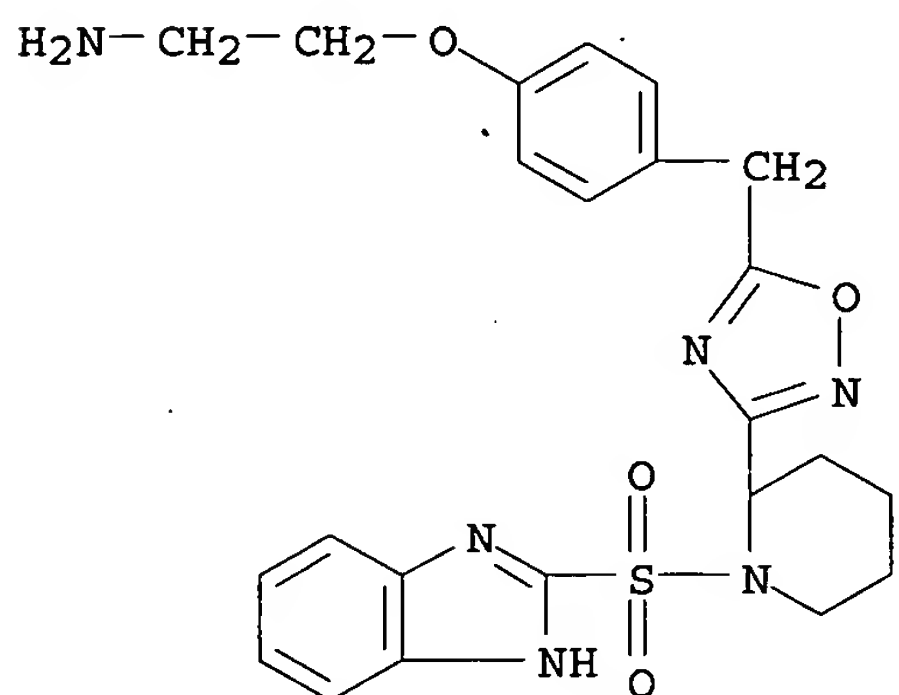
RN 242459-20-7 HCAPLUS  
 CN Piperidine, 2-[5-(cyclohexylamino)-1,3,4-oxadiazol-2-yl]-1-[(4-fluorophenyl)sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



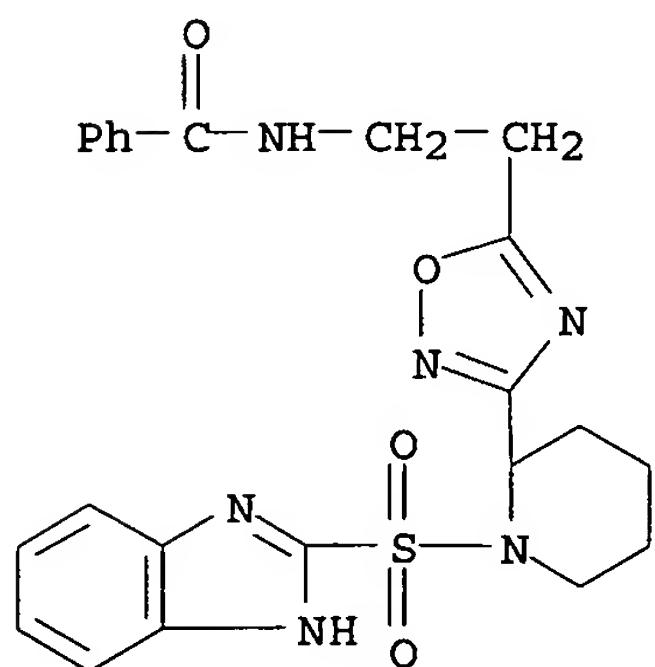
RN 242459-21-8 HCAPLUS

CN Piperidine, 2-[5-[[4-(2-aminoethoxy)phenyl]methyl]-1,2,4-oxadiazol-3-yl]-1-(1H-benzimidazol-2-ylsulfonyl)- (9CI) (CA INDEX NAME)



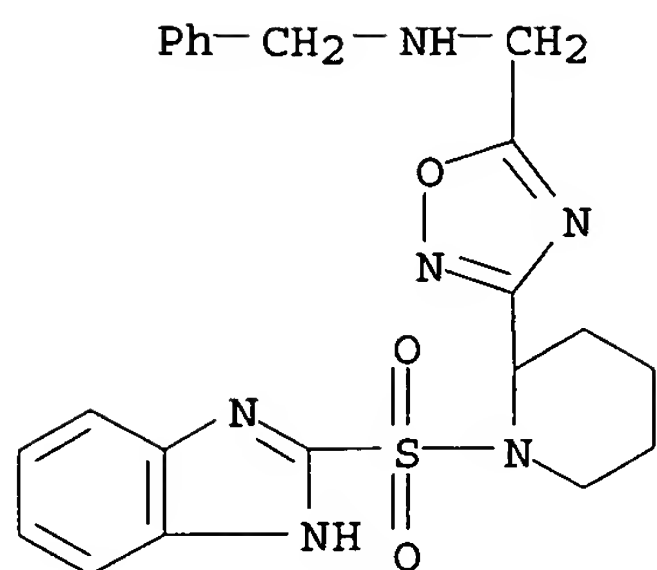
RN 242459-22-9 HCAPLUS

CN Benzamide, N-[2-[3-[1-(1H-benzimidazol-2-ylsulfonyl)-2-piperidinyl]-1,2,4-oxadiazol-5-yl]ethyl]- (9CI) (CA INDEX NAME)



RN 242459-23-0 HCAPLUS

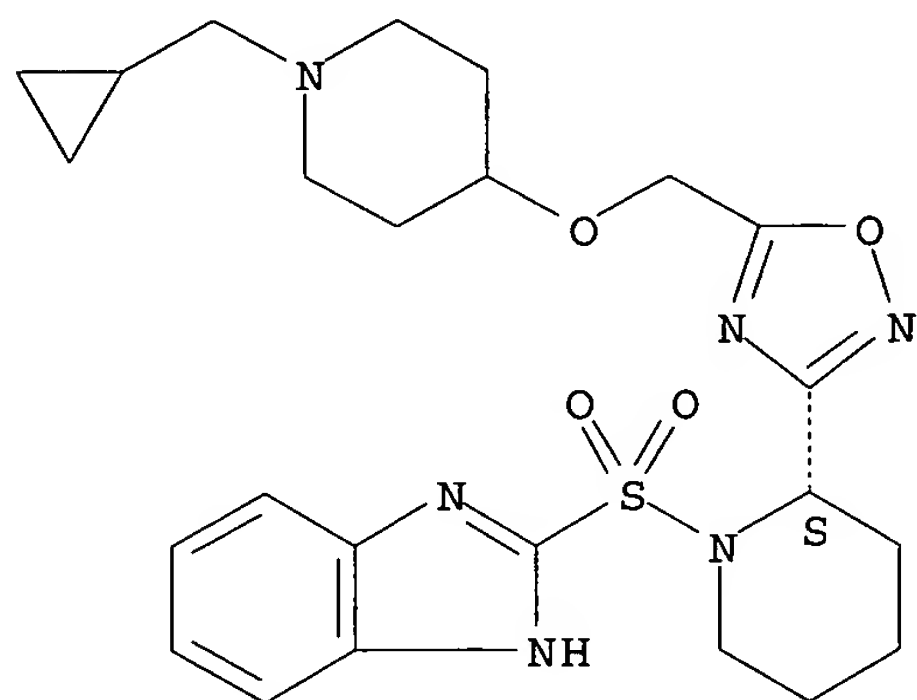
CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[[(phenylmethyl)amino]methyl]-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



RN 242459-25-2 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-[[[1-(cyclopropylmethyl)-4-piperidinyloxy]methyl]-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

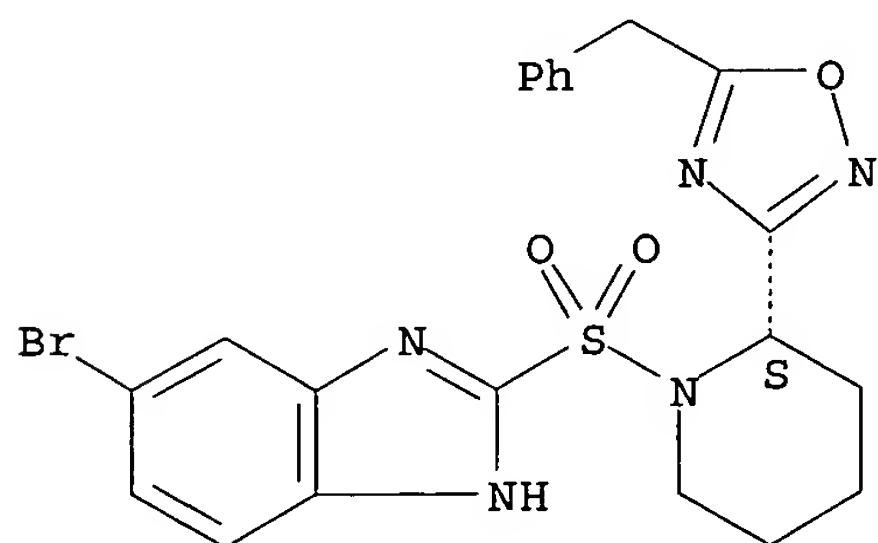
Absolute stereochemistry. Rotation (-).



RN 242459-26-3 HCAPLUS

CN Piperidine, 1-[(5-bromo-1H-benzimidazol-2-yl)sulfonyl]-2-[5-(phenylmethyl)-1,2,4-oxadiazol-3-yl]-, (2S)- (9CI) (CA INDEX NAME)

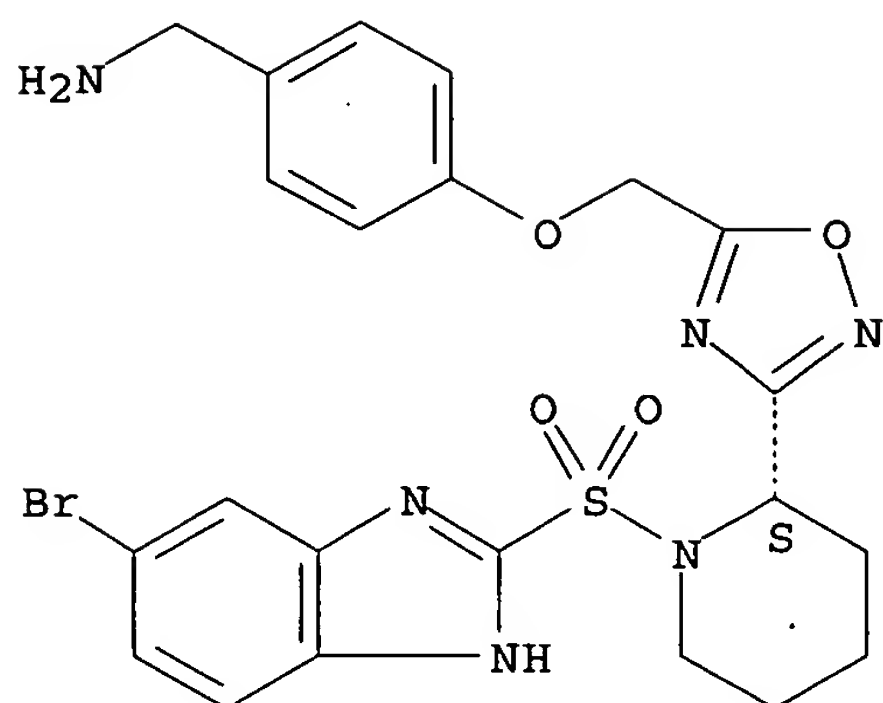
Absolute stereochemistry. Rotation (-).



RN 242459-28-5 HCAPLUS

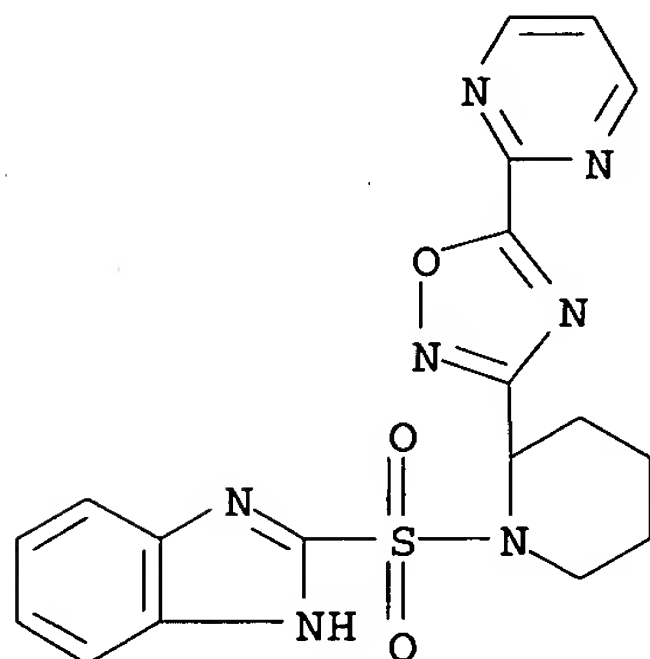
CN Piperidine, 2-[5-[[[4-(aminomethyl)phenoxy]methyl]-1,2,4-oxadiazol-3-yl]-1-[(5-bromo-1H-benzimidazol-2-yl)sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 242459-37-6 HCAPLUS

CN Piperidine, 1-(1H-benzimidazol-2-ylsulfonyl)-2-[5-(2-pyrimidinyl)-1,2,4-oxadiazol-3-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:9831 HCAPLUS

DOCUMENT NUMBER: 130:81407

TITLE: Novel tricyclic [benzocycloheptapyridine] sulfonamide inhibitors of farnesyl-protein transferase

INVENTOR(S): Njoroge, F. George; Vibulbhan, Banchar; Taveras, Arthur G.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.

PATENT ASSIGNEE(S): Schering Corporation, USA.

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9857949	A1	19981223	WO 1998-US11508	19980615 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN,				

MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ,  
 VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, ML, MR, NE, SN, TD, TG  
 ZA 9805218 A 19981215 ZA 1998-5218 19980615 <--  
 CA 2293358 AA 19981223 CA 1998-2293358 19980615 <--  
 AU 9882536 A1 19990104 AU 1998-82536 19980615 <--  
 EP 989980 A1 20000405 EP 1998-932718 19980615 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,  
 LT, LV, FI, RO  
 NZ 501619 A 20020201 NZ 1998-501619 19980615 <--  
 JP 2002507192 T2 20020305 JP 1998-547521 19980615 <--  
 MX 9912084 A 20000430 MX 1999-12084 19991217 <--  
 PRIORITY APPLN. INFO.: US 1997-877050 A 19970617  
 WO 1998-US11508 W 19980615  
 OTHER SOURCE(S): MARPAT 130:81407  
 GI

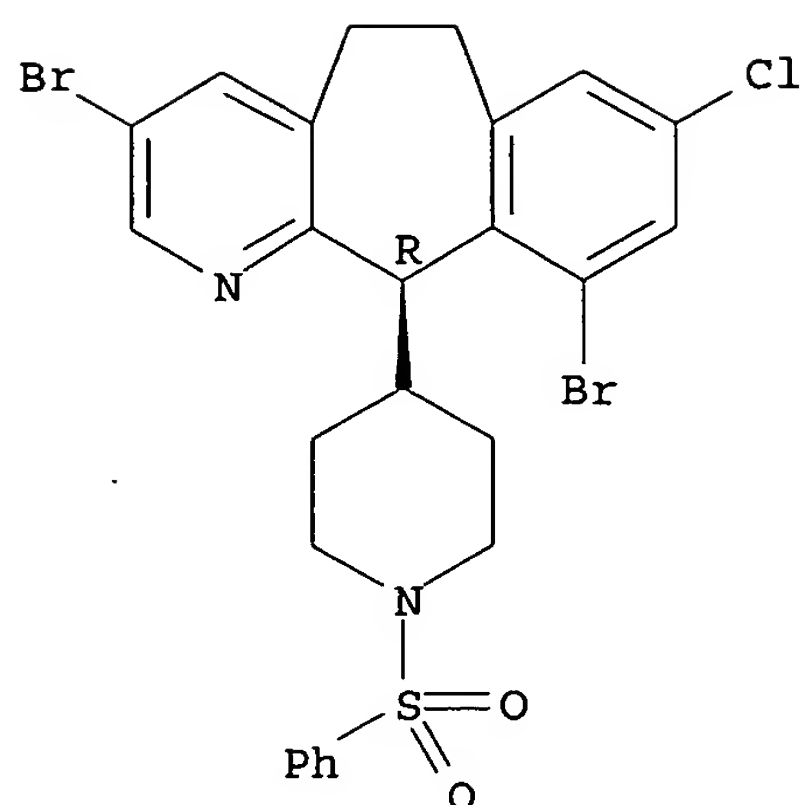
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Novel compds. I [A = N or N(O); X = C, CH or N; X1, X2 = Cl, Br, iodo; X3, X4 = H, Br, iodo, Cl, F, provided that only one is H; R5-R8 = H, alkyl, aryl, (un)substituted carbamoyl; or R5R6 and/or R7R8 = O or S; R alkyl, aryl, aralkyl, heteroaryl, cycloalkyl, (un)substituted NH2], which are **inhibitors** of the **enzyme** farnesyl protein transferase (FPT), are disclosed. Pharmaceutical compns. containing I, methods of **inhibiting** Ras function with them, and methods for **inhibiting** abnormal cell growth (i.e., treating tumor cells) with them are also disclosed. Fourteen examples were prepared. For instance, the starting material II [X3 = H] was converted to II [X3 = Cl] in 4 steps, and the latter was converted in multiple steps, ending with the sulfonylation of an N-unsubstituted piperidine derivative with MeSO<sub>2</sub>Cl in the presence of K<sub>2</sub>CO<sub>3</sub>, to give invention compound III. The latter **inhibited** Ras-CVLS farnesylation by rat brain FPT in vitro with IC<sub>50</sub> of 0.0080  $\mu$ M.

IT 218801-06-0P 218801-07-1P 218801-08-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of benzocycloheptapyridine sulfonamide derivs. as farnesyl protein transferase **inhibitors**)

RN 218801-06-0 HCAPLUS  
 CN Piperidine, 4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

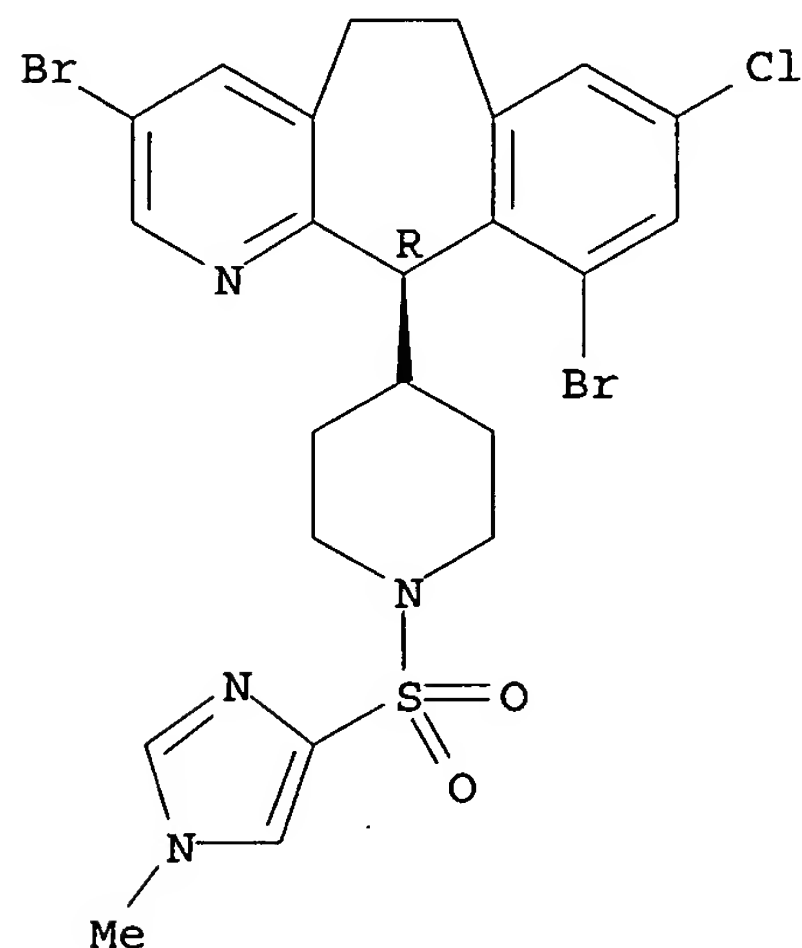
Absolute stereochemistry. Rotation (+).



RN 218801-07-1 HCAPLUS

CN Piperidine, 4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)

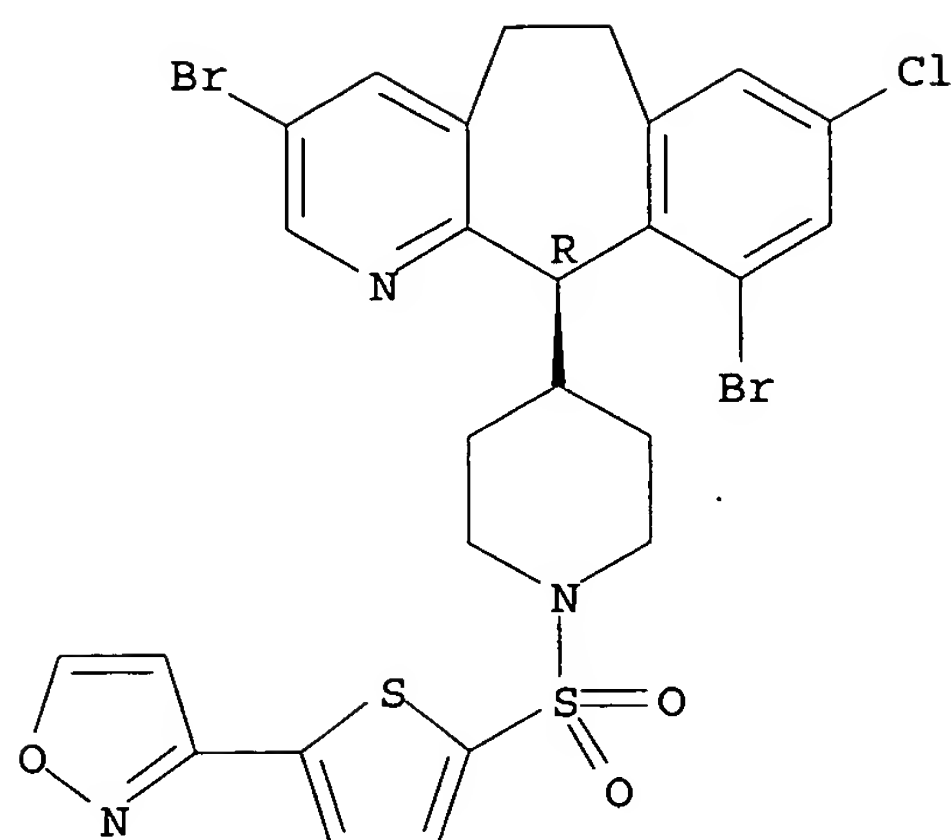
Absolute stereochemistry. Rotation (+).



RN 218801-08-2 HCAPLUS

CN Piperidine, 4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-[[5-(3-isoxazolyl)-2-thienyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:653554 HCAPLUS

DOCUMENT NUMBER: 129:290060

TITLE: Certain alpha-azacycloalkyl substituted arylsulfonamido acetohydroxamic acids, useful as **inhibitors** of matrix-degrading metalloproteinases and TNF- $\alpha$  converting **enzyme**

INVENTOR(S): Nantermet, Philippe G.; Parker, David T.; Macpherson, Lawrence J.

PATENT ASSIGNEE(S): Novartis Corporation, USA

SOURCE: U.S., 19 pp., Cont.-in-part of U.S. 5,646,167.

CODEN: USXXAM

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

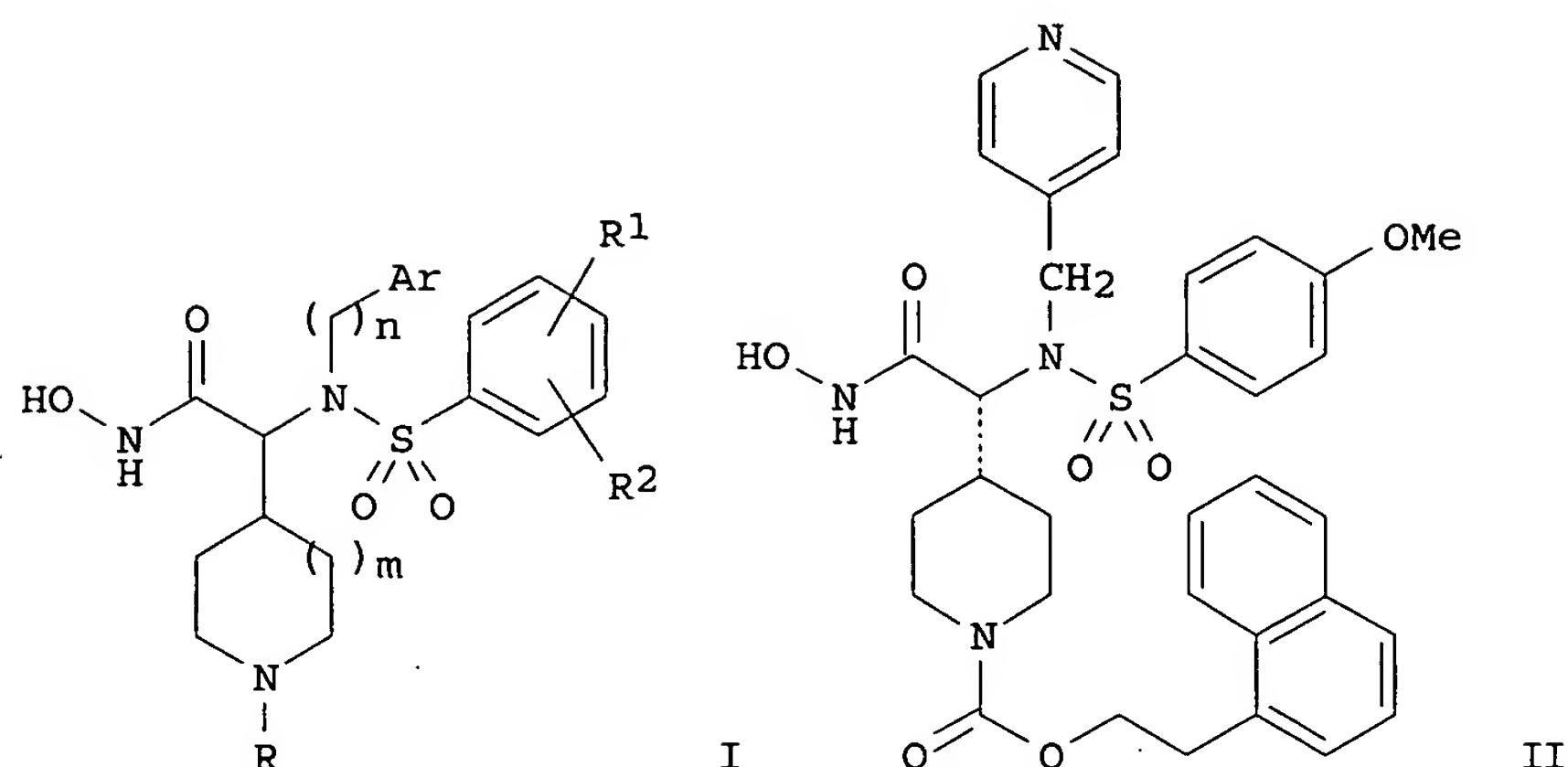
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5817822	A	19981006	US 1997-787730	19970124 <--
US 5506242	A	19960409	US 1994-265296	19940624 <--
US 5552419	A	19960903	US 1994-333676	19941103 <--
US 5646167	A	19970708	US 1995-475166	19950607 <--
PRIORITY APPLN. INFO.:			US 1994-265296	A2 19940624
			US 1994-333676	A2 19941103
			US 1995-475166	A2 19950607
			US 1993-1136	A2 19930106
			NZ 1993-250517	A 19931220

OTHER SOURCE(S): MARPAT 129:290060

GI





AB The invention relates to  $\alpha$ -(N-substituted pyrrolidinyl and piperidinyl)- $\alpha$ -(arylsulfonamido)acetohydroxamic acids I [R = acyl derived from a carboxylic, carbonic, or carbamic acid; or R = (lower alkyl, aryl-lower alkyl, or aryl)-sulfonyl, di-(aryl-lower alkyl or alkyl)-aminosulfonyl, or aryl-lower alkyl; Ar = carbocyclic aryl, heterocyclic aryl, or biaryl; R1 and R2 = H, alkyl, alkoxy, halo, OH, acyloxy, alkoxy-lower alkoxy, CF3, or cyano; or R1R2 = alkylenedioxy; m = 0 or 1; n = 1-5] and their pharmaceutically acceptable prodrugs and salts. Also disclosed are a process for the preparation of the compds., pharmaceutical compns. comprising them, and their use for therapeutic treatment or manufacture of a pharmaceutical composition. Approx. 70 invention compds. and various starting materials and intermediates are described. For instance, benzyl 2-(R)-[(4-methoxybenzenesulfonyl)(4-picolyl)amino]-2-(4-piperidinyl)acetate dihydrochloride (prepared in approx. 9 steps) was condensed at the piperidine N with 1-naphthaleneethanol and di(2-pyridyl) carbonate (phosgene equivalent), and the product underwent hydrogenolysis of the benzyl ester, amidation with tert-BuONH2, and removal of the tert-Bu group with dry HCl, to give title salt II.HCl. In a test for inhibition of production of soluble TNF- $\alpha$  by LPS-stimulated THP-1 cells in vitro, II.HCl had an IC50 of 0.7  $\mu$ M. II.HCl also inhibited the in-vitro hydrolysis of substance P by stromelysin with an IC50 of approx. 15 nM.

IT 214217-61-5P

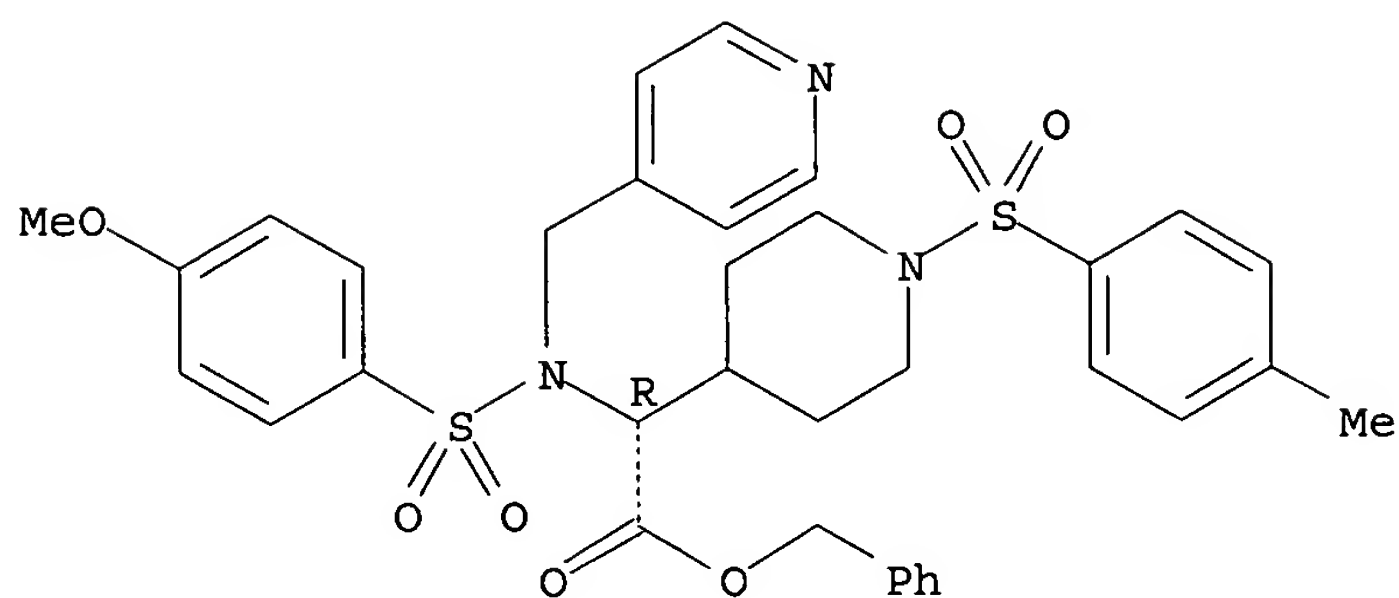
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of azacycloalkyl arylsulfonamido acetohydroxamic acids as **inhibitors** of matrix-degrading metalloproteinases and TNF- $\alpha$  converting **enzyme**)

RN 214217-61-5 HCAPLUS

CN 4-Piperidineacetic acid,  $\alpha$ -[[[(4-methoxyphenyl)sulfonyl](4-pyridinylmethyl)amino]-1-[(4-methylphenyl)sulfonyl]-, phenylmethyl ester, ( $\alpha$ R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:611997 HCAPLUS

DOCUMENT NUMBER: 129:260344

TITLE: Preparation of sulfonyl divalent aryl or heteroaryl hydroxamic acid compounds as inhibitors of matrix metalloprotease

INVENTOR(S): Mcdonald, Joseph J.; Barta, Thomas E.; Becker, Daniel P.; Bedell, Louis J.; Rao, Shashidhar N.; Freskos, John N.; Mischke, Brent V.

PATENT ASSIGNEE(S): Monsanto Company, USA

SOURCE: PCT Int. Appl., 130 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 10

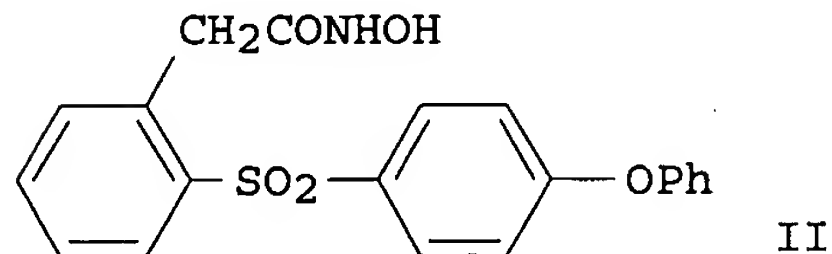
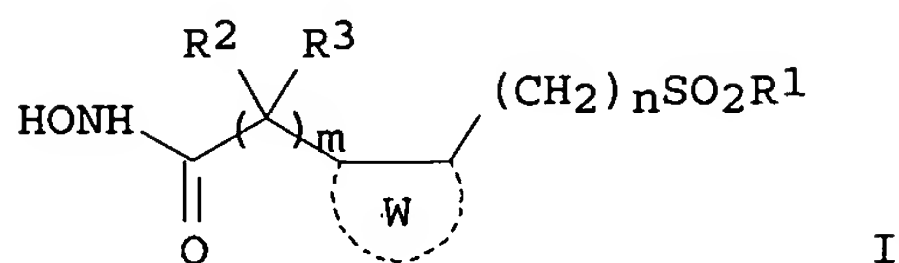
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9838859	A1	19980911	WO 1998-US4300	19980304 <--
W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2283275	AA	19980911	CA 1998-2283275	19980304 <--
AU 9865424	A1	19980922	AU 1998-65424	19980304 <--
AU 750130	B2	20020711		
EP 973392	A1	20000126	EP 1998-911481	19980304 <--
EP 973392	B1	20031119		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
BR 9808166	A	20000516	BR 1998-8166	19980304 <--
NZ 337326	A	20010525	NZ 1998-337326	19980304 <--
JP 2001518081	T2	20011009	JP 1998-538799	19980304 <--
CN 1105114	B	20030409	CN 1998-804575	19980304 <--
AT 254599	E	20031215	AT 1998-911481	19980304
PT 973392	T	20040430	PT 1998-911481	19980304
ES 2206903	T3	20040516	ES 1998-911481	19980304
ES 2209122	T3	20040616	ES 1998-910177	19980304
US 2001020021	A1	20010906	US 1999-230209	19990624 <--
US 6380258	B2	20020430		

NO 9904252	A	19990902	NO 1999-4252	19990902 <--
NO 315647	B1	20031006		
MX 9908156	A	20000228	MX 1999-8156	19990903 <--
US 2003191317	A1	20031009	US 2000-728408	20001201 <--
US 6794511	B2	20040921		
US 2003073845	A1	20030417	US 2001-909227	20010719 <--
US 6696449	B2	20040224		
US 2002103239	A1	20020801	US 2001-997552	20011129 <--
US 6656954	B2	20031202		
US 2005075374	A1	20050407	US 2004-867391	20040614
PRIORITY APPLN. INFO.:			US 1997-35182P	P 19970304
			WO 1998-US4300	W 19980304
			US 1999-310813	B1 19990512
			US 1999-230209	A2 19990624
			US 2000-569034	A2 20000511
			US 2000-728408	A2 20001201

OTHER SOURCE(S): MARPAT 129:260344

GI



AB Sulfonyl divalent aromatic or heteroarom. ring hydroxamic acid compds. (I; m, n = 0 or 1 and m+n = 1; R1 = a substituent containing a 5- or 6-membered cyclohydrocarbyl, heterocyclyl, aryl, or heteroaryl radical bonded directly to the depicted SO2-group and having a length greater than about that of a hexyl group and less than about that of an eicosyl group; R1 defines a three-dimensional volume, when rotated about an axis drawn through the SO2-bonded 1-position and the center of 3,4-bond of a 5-membered ring radical, whose widest dimension in a direction transverse to the axis of rotation is about that of one furanyl ring to about that of two Ph rings; R2, R3 = hydrido, C1-4 hydrocarbyl, OH, or NH2 or R2 and R3 together with the depicted carbon atom to which they are bonded from a 6-membered heterocyclic ring containing O, S, or N heteroatom, said heteroatom being optionally substituted with one or two O atoms when sulfur and being optionally substituted with a moiety selected from the group consisting of a C1-4 hydrocarbyl, C3-6 cyclohydrocarbyl, C1-4 acylhydrocarbyl, and sulfonyl-C1-4 hydrocarbyl when nitrogen) that inter alia **inhibits** matrix metalloprotease activity are disclosed. Also disclosed is a treatment process that comprises administering a contemplated sulfonyl divalent aromatic or heteroarom. ring hydroxamic acid compound in an MMP **enzyme-inhibiting** effective amount to a host having a condition associated with pathol. matrix metalloprotease activity. Thus, 2-fluorobenzaldehyde was condensed with 4-phenoxybenzenethiol in the

presence of K<sub>2</sub>CO<sub>3</sub> under reflux for 20 h to give 2-(4-phenoxyphenylthio)benzaldehyde (II). Tetra-Et dimethylammoniomethylenediphosphonate was treated with NaH in THF and then condensed with II at ambient temperature for 4 h to give [2-(4-phenoxyphenylthio)phenyl]acetic acid which was oxidized with a mixture of 30% H<sub>2</sub>O<sub>2</sub> and AcOH at 100° for 40 min to give [2-(4-phenoxyphenylsulfonyl)phenyl]acetic acid. The latter compound was condensed with O-tetrahydropyranylhydroxylamine using EDC in MeCN followed by treatment with p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H in MeOH to give the title compound (III), which showed IC<sub>50</sub> of 2, 900, and 0.3 nM against MMP-13, MMP-1, and MMP-2, resp.

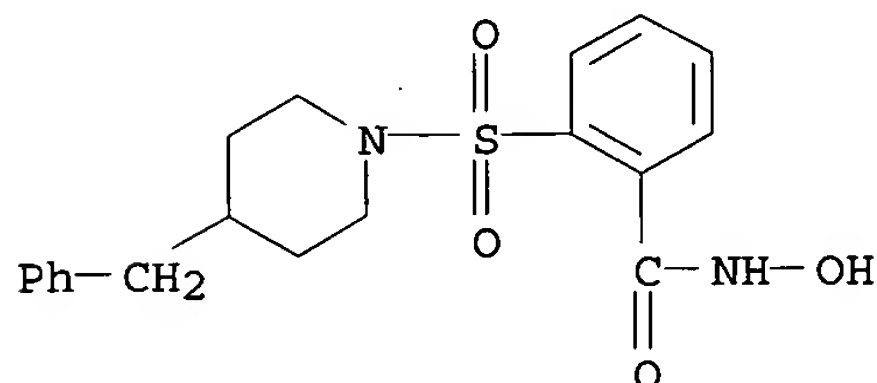
IT 213012-59-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sulfonyl divalent aryl or heteroaryl hydroxamic acid compds. as **inhibitors** of matrix metalloprotease)

RN 213012-59-0 HCAPLUS

CN Benzamide, N-hydroxy-2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI)  
(CA INDEX NAME)



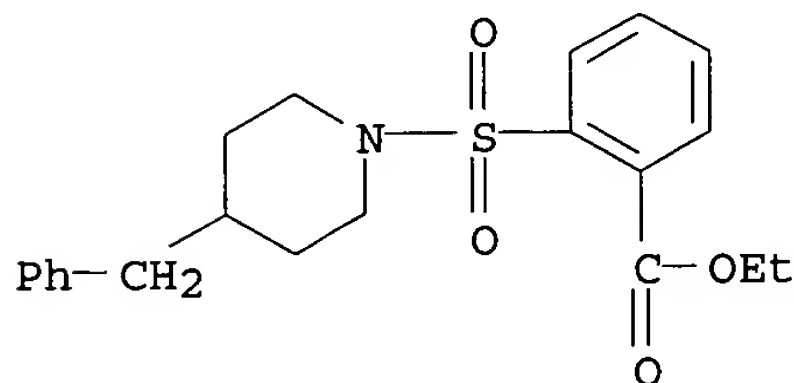
IT 213012-83-0P 213012-84-1P 213012-85-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of sulfonyl divalent aryl or heteroaryl hydroxamic acid compds. as **inhibitors** of matrix metalloprotease)

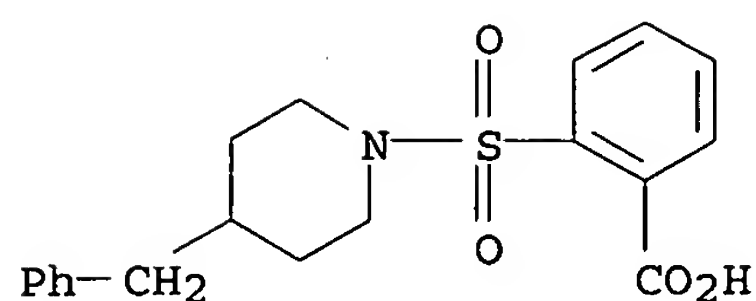
RN 213012-83-0 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-, ethyl ester  
(9CI) (CA INDEX NAME)



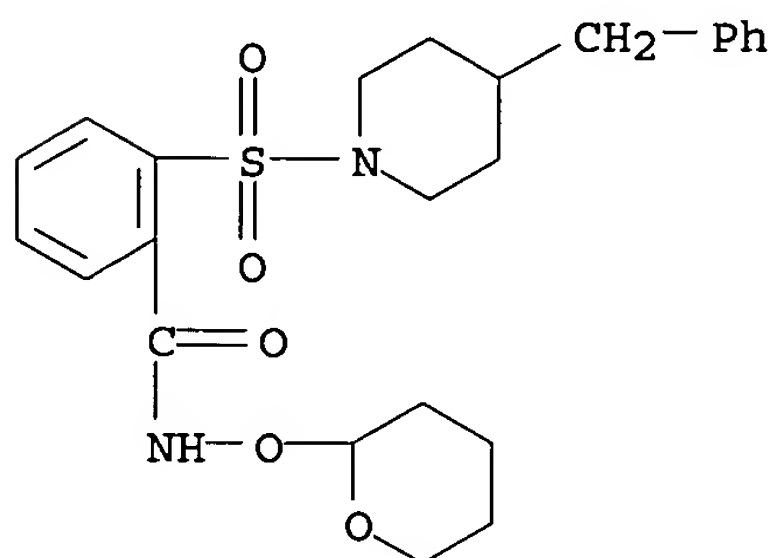
RN 213012-84-1 HCAPLUS

CN Benzoic acid, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 213012-85-2 HCAPLUS

CN Benzamide, 2-[[4-(phenylmethyl)-1-piperidinyl]sulfonyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:251152 HCAPLUS

DOCUMENT NUMBER: 128:321926

TITLE:- Preparation of aspartate ester inhibitors of interleukin-1 $\beta$  converting enzyme

INVENTOR(S): Albrecht, Hans P.; Allen, Hamish John; Brady, Kenneth Dale; Caprathe, Bradley William; Gilmore, John Lodge; Harter, William Glen; Hays, Sheryl Jeanne; Kostlan, Catherine Rose; Lunney, Elizabeth Ann; Para, Kimberly Suzanne; et al.

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 179 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

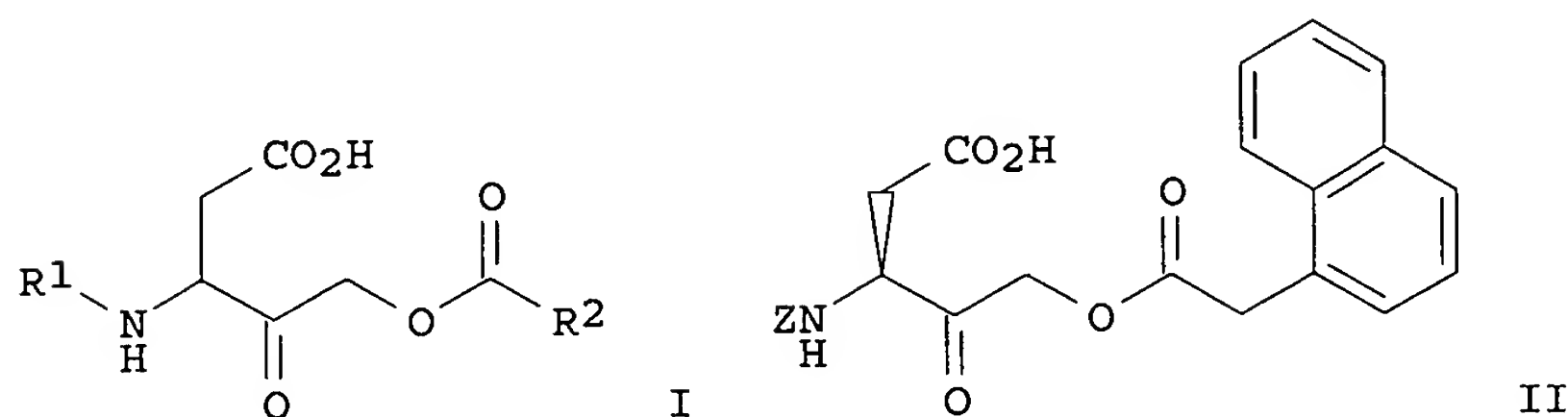
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816502	A1	19980423	WO 1997-US18514	19971009 <--
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2268098	AA	19980423	CA 1997-2268098	19971009 <--
AU 9749023	A1	19980511	AU 1997-49023	19971009 <--
AU 738341	B2	20010913		

EP 932598 A1 19990804 EP 1997-911715 19971009 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 BR 9712530 A 19991019 BR 1997-12530 19971009 <--  
 JP 2001506974 T2 20010529 JP 1998-518519 19971009 <--  
 NO 9901677 A 19990609 NO 1999-1677 19990409 <--  
 KR 2000049048 A 20000725 KR 1999-703117 19990410 <--  
 PRIORITY APPLN. INFO.: US 1996-28322P P 19961011  
 WO 1997-US18514 W 19971009  
 OTHER SOURCE(S): MARPAT 128:321926  
 GI



AB The present invention relates to compds. I [R1 = carboxy, acyl, amino acid residue, etc.; R2 = (CR2)n-X-R3; each R = independently H, C1-6 alkyl, OH; R3 = (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, cycloalkyl, etc; X = bond, O, S; n = 0-3; and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof] as **inhibitors** of interleukin-1 $\beta$  converting **enzyme** (ICE). This invention also relates to a method of treatment of stroke, inflammatory diseases, reperfusion injury, Alzheimer's disease, and shigellosis, and to a pharmaceutically acceptable composition that contains a compound that is an **inhibitor** of interleukin-1 $\beta$  converting **enzyme**. Thus, substitution of Z-Asp(OCMe3)-CH2Br (Z = PhCH2O2C) with 1-naphthylacetic acid, followed by acidic deprotection, gave desired aspartate ester derivative II. II **inhibited** ICE with Ki = 0.460  $\mu$ M and IC50 = 3.100  $\mu$ M, and **inhibited** Ich-2 (caspase-4) with IC50 = 3.60  $\mu$ M, as determined using in vitro assays. Related prepared compds. I (196 examples) were also tested for ICE **inhibition** (Ki values of 0.00008 to 76  $\mu$ M and IC50 values of 0.0013 to 32  $\mu$ M), and Ich-2 **inhibition** (IC50 = 0.021 to 76  $\mu$ M).

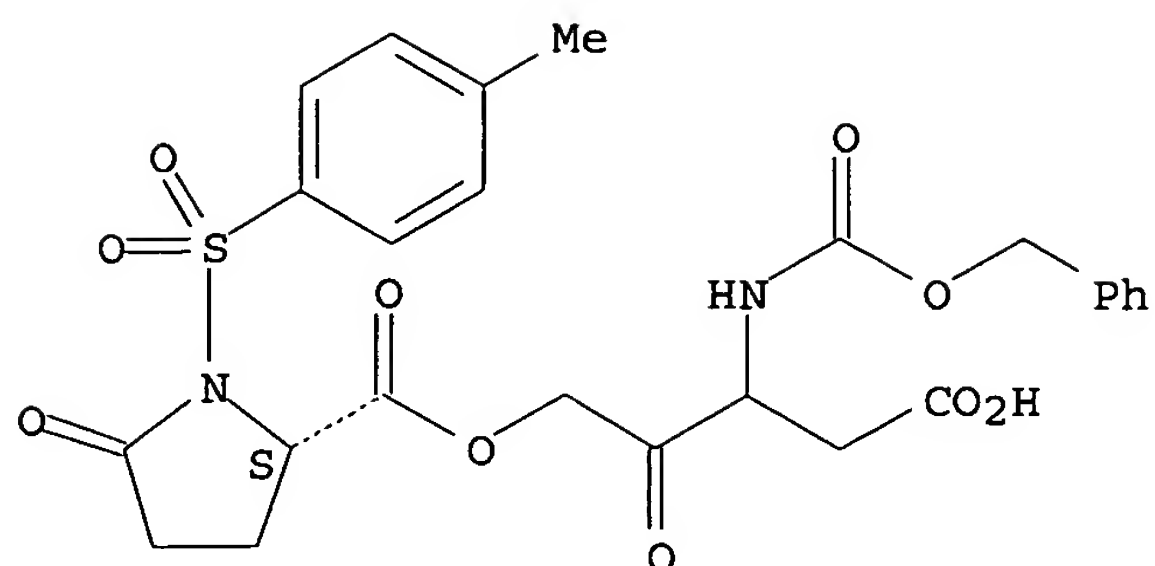
IT 206863-33-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of aspartate ester **inhibitors** of interleukin-1 $\beta$  converting **enzyme**)

RN 206863-33-4 HCAPLUS

CN L-Proline, 1-[(4-methylphenyl)sulfonyl]-5-oxo-, 4-carboxy-2-oxo-3-[[phenylmethoxy]carbonylamino]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:146700 HCAPLUS

DOCUMENT NUMBER: 128:213393

TITLE: Method of using neurotrophic sulfonamide compounds

INVENTOR(S) : Hamilton, Gregory S.; Li, Jia-he; Steiner, Joseph P.

PATENT ASSIGNEE(S): GPI NIL Holdings, Inc., USA

SOURCE: U.S., 14 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

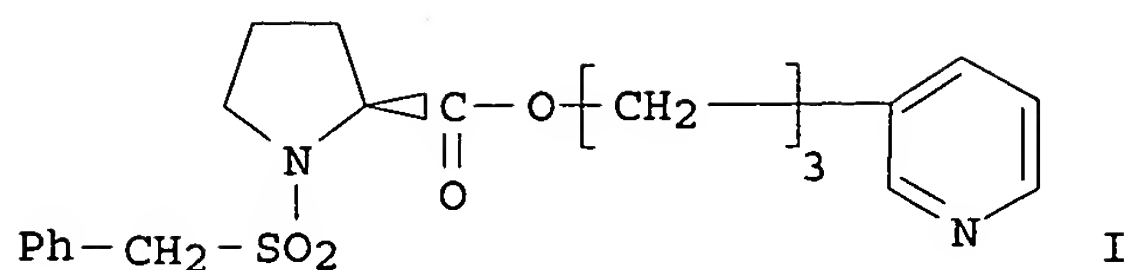
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5721256	A	19980224	US 1997-799407	19970212 <--
ZA 9800824	A	19981030	ZA 1998-824	19980202 <--
CA 2280742	AA	19980820	CA 1998-2280742	19980211 <--
WO 9835675	A1	19980820	WO 1998-US2215	19980211 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9862688	A1	19980908	AU 1998-62688	19980211 <--
EP 1014978	A1	20000705	EP 1998-904939	19980211 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2001511806	T2	20010814	JP 1998-535815	19980211 <--
US 5968957	A	19991019	US 1998-28517	19980223 <--
MX 9907384	A	20000731	MX 1999-7384	19990810 <--
US 6245783	B1	20010612	US 1999-419801	19991018 <--
US 2003114492	A1	20030619	US 2001-814954	20010323 <--
RITY APPLN. INFO.:			US 1997-799407	A 19970212
			WO 1998-US2215	W 19980211
			US 1998-28517	A3 19980223
			US 1999-419801	A1 19991018

OTHER SOURCE(S) :                    MARPAT 128:213393

GI





AB Low-mol.-weight sulfonamides, e.g. I, having an affinity for FKBP-type immunophilins and thus **inhibitors** of the **enzyme** activity associated with immunophilin proteins, particularly peptidyl-prolyl isomerase (rotamase), are useful for the treatment of neurol. disorders including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. An example was given for the preparation of I.

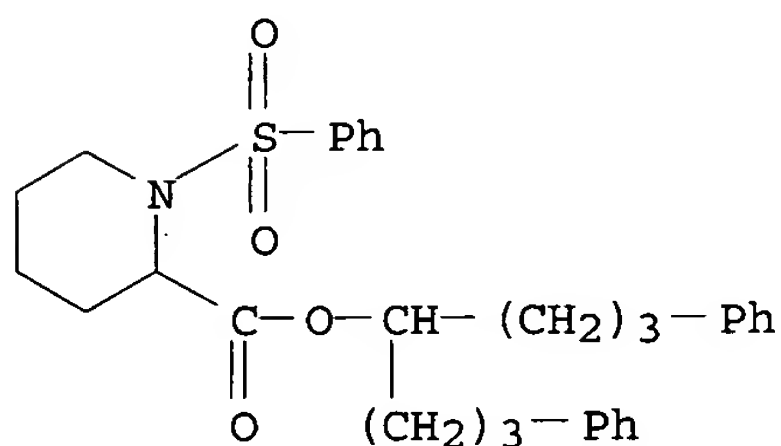
IT 204332-48-9 204332-49-0 204332-50-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(rotamase-inhibiting sulfonamides for treatment of neurol. disorders)

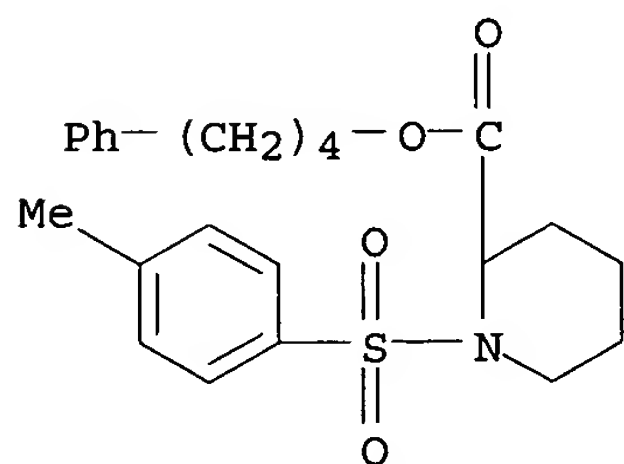
RN 204332-48-9 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(phenylsulfonyl)-, 4-phenyl-1-(3-phenylpropyl)butyl ester (9CI) (CA INDEX NAME)



RN 204332-49-0 HCAPLUS

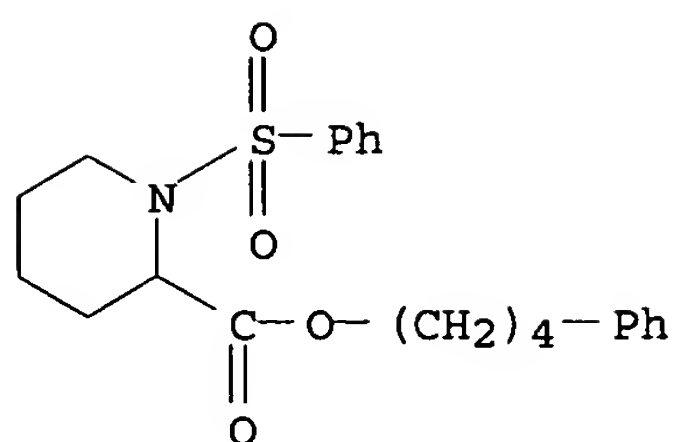
CN 2-Piperidinecarboxylic acid, 1-[(4-methylphenyl)sulfonyl]-, 4-phenylbutyl ester (9CI) (CA INDEX NAME)



RN 204332-50-3 HCAPLUS

CN 2-Piperidinecarboxylic acid, 1-(phenylsulfonyl)-, 4-phenylbutyl ester (9CI) (CA INDEX NAME)





REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:112229 HCAPLUS

DOCUMENT NUMBER: 128:192667

TITLE: Preparation of substituted aromatic compounds as inhibitors of tumor necrosis factor and cyclic AMP phosphodiesterase

INVENTOR(S): He, Wei; Hulme, Christopher; Huang, Fu-chih; Djuric, Stevan W.; Moriarty, Kevin; Labaudiniere, Richard

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA; He, Wei; Hulme, Christopher; Huang, Fu-Chih; Djuric, Stevan W.; Moriarty, Kevin; Labaudiniere, Richard

SOURCE: PCT Int. Appl., 154 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805327	A1	19980212	WO 1997-US13343	19970722 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738990	A1	19980225	AU 1997-38990	19970722 <--
PRIORITY APPLN. INFO.:			US 1996-23165P	P 19960805
			WO 1997-US13343	W 19970722
OTHER SOURCE(S):		MARPAT 128:192667		
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB This invention is directed to compound of formula [I; ring A = Q10, Q11; Ar1 = Q12, Q13, Q14; ring Ar2 = (un)substituted fused Ph or fused monocyclic heteroaryl; R = (un)substituted alkyl, aralkyl, or heteroaralkyl, arylsulfonyl, heteroarylsulfonyl, etc.; R1 = carboxyalkyl, alkoxycarbonylalkyl, N-(un)substituted carbamoylalkyl, cyanoalkyl,

(un)substituted aralkyl or heteroaralkyl; R2 = (un)substituted lower alkyl; R3 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, or oxaaliph., (un)substituted or optionally oxidized cyclothioalkyl or cyclothioalkenyl; R4, R6 = H, (un)substituted lower alkyl; R5 = (un)substituted alkyl, alkoxy, cycloalkyl, or heterocyclyl, alkoxycarbonyl, cyano, (un)substituted carbamoyl, (un)substituted aryl or heteroaryl, or CO<sub>2</sub>H where m is other than 0; R7 = H, alkoxy, (un)substituted cycloalkyl, cycloalkenyl, cycloalkoxy, cycloalkenyloxy, aryl, heteroaryl, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, alkylthio, or alkylsulfanyl, etc.; Q1, Q2 = CH<sub>2</sub>, O-(un)substituted CHOH, CO; Q3, Q4, Q5, Q9 = N, optionally halo-substituted CH; Q6 = N, CH; Q7-C-Q8 = N-(un)saturated NHCH:N, O-CH:CH, CH:CH-O, O-CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>O; Z', Z'' = H or Z'Z'' = O or S; Z1, Z2 = direct bond, O, S; Z3 = SO<sub>2</sub>, direct bond; Z4 = direct bond, O, S, NH; Z5 = direct bond, (un)substituted lower alkenyl; m, n = 0, 1; p = 1-3; q = 0-5] or hydrate, solvate, N-oxide, or prodrug thereof or a pharmaceutically acceptable salt thereof are. They are especially useful for **inhibiting** the production or physiol. effects of tumor necrosis factor (TNF) and **inhibit** cAMP phosphodiesterase and are useful for the treatment of disease states associated with abnormally high physiol. levels of cytokines such as TNF or those associated with pathol. (e.g. asthma as bronchodilators or inflammation) conditions that are modulated by **inhibiting enzymes** such as cAMP phosphodiesterase (no data). In particular, they are used for treating a disease state capable of being modulated by **inhibiting** TNF, e.g., joint inflammation, arthritis, rheumatoid arthritis, rheumatoid spondylitis and osteoarthritis, sepsis, septic shock, gram neg. sepsis, toxic shock syndrome, acute respiratory distress syndrome, asthma, bone resorption diseases, reperfusion injury, graft vs. host reaction, allograft rejection malaria, myalgias, HIV, AIDS, cachexia, Crohn's disease, ulcerative colitis, pyresis, systemic lupus erythematosus, multiple sclerosis, type I diabetes mellitus, psoriasis, Behcet's disease, anaphylactoid purpura nephritis, chronic glomerulonephritis, inflammatory bowel disease, and leukemia. They are also used for treating a pathol. condition associated with a function of cAMP phosphodiesterase, eosinophil accumulation or function of the eosinophil, e.g., asthma, atopic dermatitis, urticaria, allergic rhinitis, psoriasis, rheumatic arthritis, ulcerative colitis, Crohn's disease, adult respiratory distress syndrome, diabetes insipidus, keratosis, dermatitis, cerebral senility, multiinfarct dementia, senile dementia, memory impairment associated with Parkinson's disease, cardiac arrest, stroke, and intermittent claudication. The present invention is also directed to their pharmaceutical use, pharmaceutical compns. containing the compds., and methods of their preparation. Thus, 2-(3-cyclopentyloxy-4-methoxyphenyl)-5-hydroxymethyl-2-(4-pyridylmethyl)indan-1,3-dione was treated with NaH in THF, tosylated by tosyl chloride at 0° to room temperature for 2 h, and then condensed with 1-methylpiperazine in the K<sub>2</sub>CO<sub>3</sub> in acetone at room temperature for 4 days the presence of K<sub>2</sub>CO<sub>3</sub> in acetone to give the title compound, piperazinylmethylpyridylmethylindandione derivative (II).

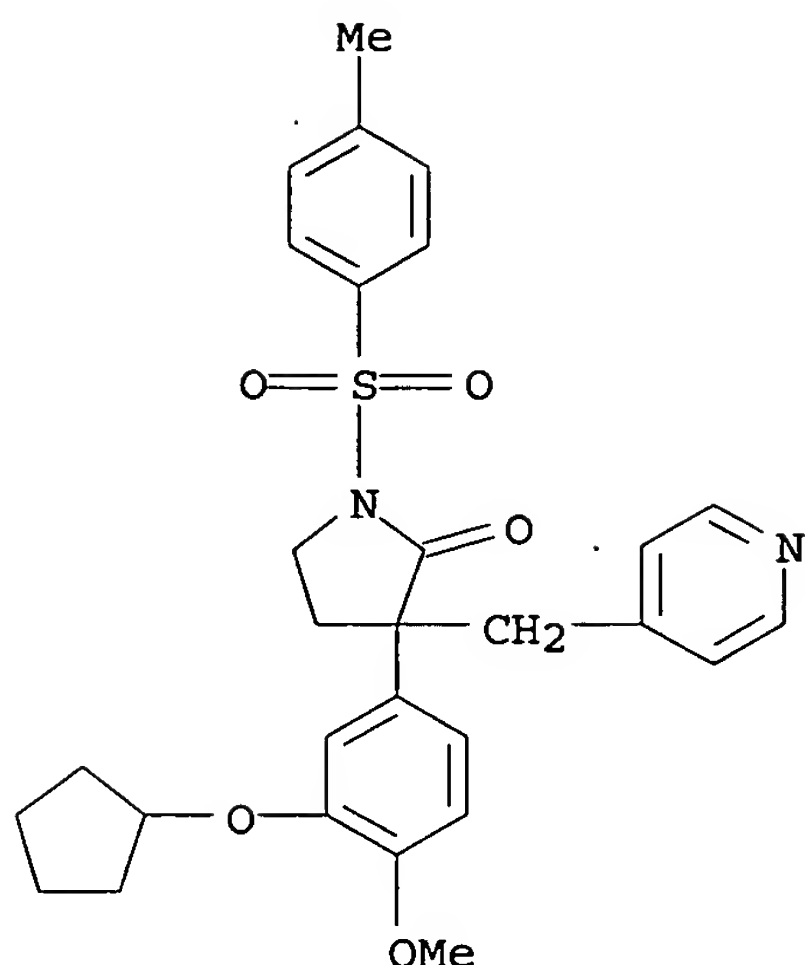
IT 203441-35-4P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted aromatic compds. as **inhibitors** of tumor necrosis factor and cAMP phosphodiesterase)

RN 203441-35-4 HCAPLUS

CN 2-Pyrrolidinone, 3-[3-(cyclopentyloxy)-4-methoxyphenyl]-1-[(4-methylphenyl)sulfonyl]-3-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:132788 HCAPLUS

DOCUMENT NUMBER: 126:141390

TITLE: Primer extension assays for detection of nucleases producing single-stranded nucleic acids and the screening of inhibitors

INVENTOR(S): Cole, James L.; Kuo, Lawrence C.; Olsen, David B.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640994	A1	19961219	WO 1996-US8330	19960603 <--
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2222688	AA	19961219	CA 1996-2222688	19960603 <--
EP 833945	A1	19980408	EP 1996-920611	19960603 <--
EP 833945	B1	20020130		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11506607	T2	19990615	JP 1996-500964	19960603 <--
AT 212676	E	20020215	AT 1996-920611	19960603 <--
ES 2170861	T3	20020816	ES 1996-920611	19960603 <--
US 6100028	A	20000808	US 1998-973139	19980731 <--
PRIORITY APPLN. INFO.:			US 1995-487760	A 19950607
			WO 1996-US8330	W 19960603

AB An assay for **enzymes** that act on substrates to produce a single-stranded oligonucleotide product has been developed. The method uses DNA polymerase-catalyzed extension of the oligonucleotide cleavage product using labeled nucleotides and a DNA template containing a 3' region complementary to the oligonucleotide product joined to a 5' region

consisting of repeated nucleotide residues. The DNA polymerase extension assay does not involve gel electrophoretic separation and is amenable to high volume screening of potential **inhibitors**. Other key features of the assay are that it monitors the substrate cleavage reaction only at the correct position in the sequence, thereby discriminating against nonspecific cleavage products, and that it is sensitive enough to detect 200 amol of product.

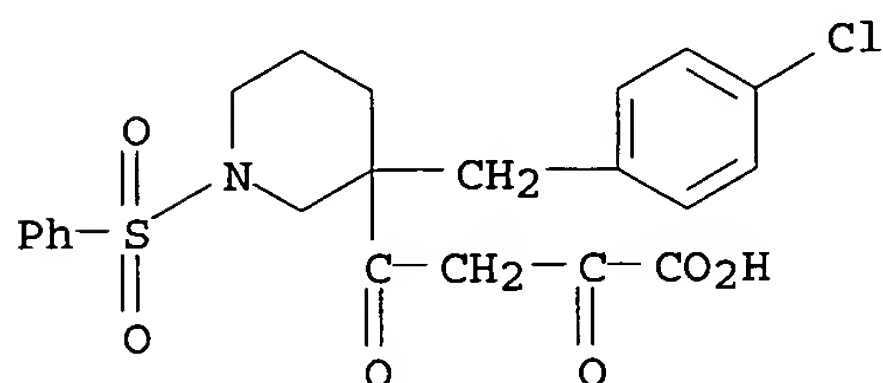
IT 186460-35-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**inhibition** of influenza virus endonuclease by; primer extension assays for detection of nucleases producing single-stranded nucleic acids and screening of **inhibitors**)

RN 186460-35-5 HCAPLUS

CN 3-Piperidinebutanoic acid, 3-[(4-chlorophenyl)methyl]- $\alpha,\gamma$ -dioxo-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



L32 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:559909 HCAPLUS

DOCUMENT NUMBER: 119:159909

TITLE: Aromatic sulfonamide derivative **inhibitors** of calcium-dependent **enzymes** and phospholipase A2

INVENTOR(S): Dumont, Raymond

PATENT ASSIGNEE(S): Pharno-Wedropharm G.m.b.H., Germany

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

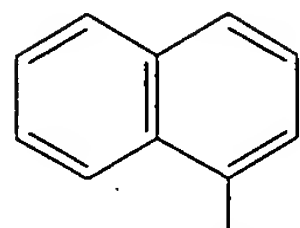
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9305014	A1	19930318	WO 1991-EP1678	19910905 <--
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9184307	A1	19930405	AU 1991-84307	19910905 <--
EP 602028	A1	19940622	EP 1991-915001	19910905 <--
EP 602028	B1	19960117		
R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 06510017	T2	19941110	JP 1991-513470	19910905 <--
JP 3176619	B2	20010618		
ES 2084176	T3	19960501	ES 1991-915001	19910905 <--
US 5663174	A	19970902	US 1997-785251	19970117 <--
PRIORITY APPLN. INFO.:			EP 1991-915001	A 19910905

WO 1991-EP1678  
US 1994-204317

A 19910905  
B1 19940304

OTHER SOURCE(S) : MARPAT 119:159909  
GI



SO<sub>2</sub>NH(CH<sub>2</sub>Ph)CONH(CH<sub>2</sub>)<sub>6</sub>NH<sub>2</sub> I

AB Aromatic sulfonamides ZSO<sub>2</sub>ANR<sub>1</sub>R<sub>2</sub> [A = direct bond, amino acid residue with its N atom bound to the SO<sub>2</sub> moiety and the carboxyl group bound to the N-atom moiety; R<sub>1</sub> = H; R<sub>2</sub> = biphenyl, C<sub>2</sub>-6 alkylene, Ph (only if Z ≠ naphthyl or chloronaphthyl and A ≠ direct bond); R<sub>1</sub>R<sub>2</sub> may form a piperazine ring], useful as **inhibitors** of phospholipase A<sub>2</sub> and calcium-dependent **enzymes**, and which may be of use in the treatment of inflammation, infarct, and arthritis (no data), are prepared. Thus, the HCl salt of sulfonamide I, prepared from chloronaphthalenesulfonyl chloride, N-tert-BOC-L-phenylalanine, and N-BOC-6-aminohexane, exhibited 50% **inhibition** concentration of bovine pancreatic phospholipase A<sub>2</sub> at 67 μm.

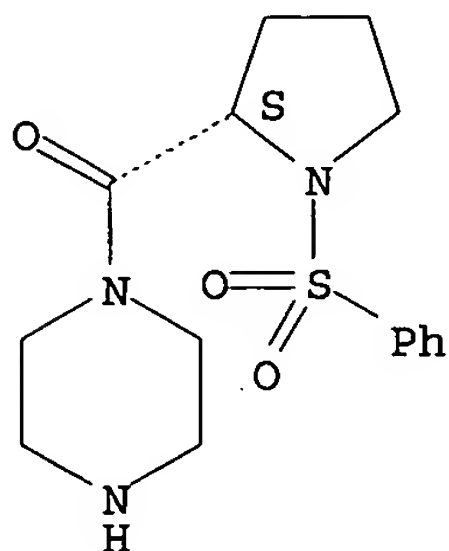
IT 149569-25-5P 149569-31-3P 149569-33-5P  
149569-39-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and calcium-dependent **enzyme** and phospholipase A<sub>2</sub>  
**inhibitory** activity of)

RN 149569-25-5 HCAPLUS

CN Piperazine, 1-[[1-(phenylsulfonyl)-2-pyrrolidinyl]carbonyl]-,  
monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

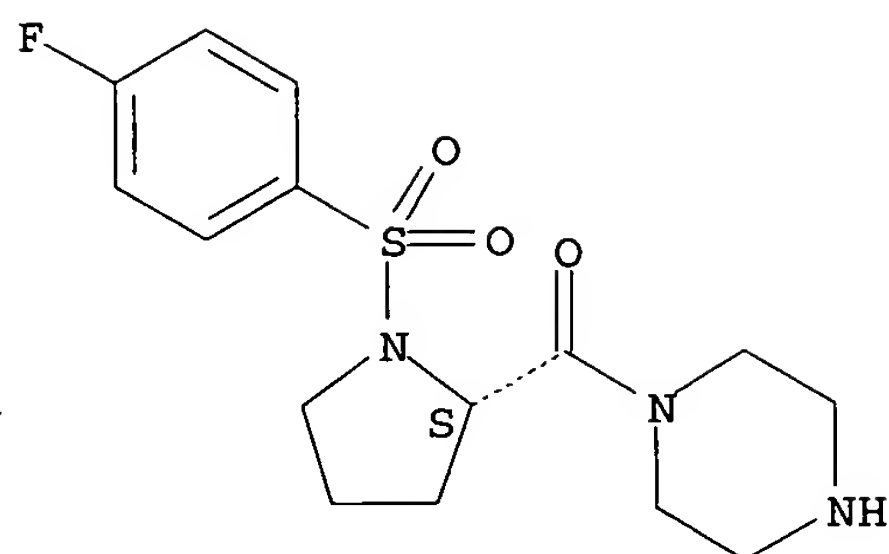


● HCl

RN 149569-31-3 HCAPLUS

CN Piperazine, 1-[[1-[(4-fluorophenyl)sulfonyl]-2-pyrrolidinyl]carbonyl]-,  
monohydrochloride, (S)- (9CI) (CA INDEX NAME)

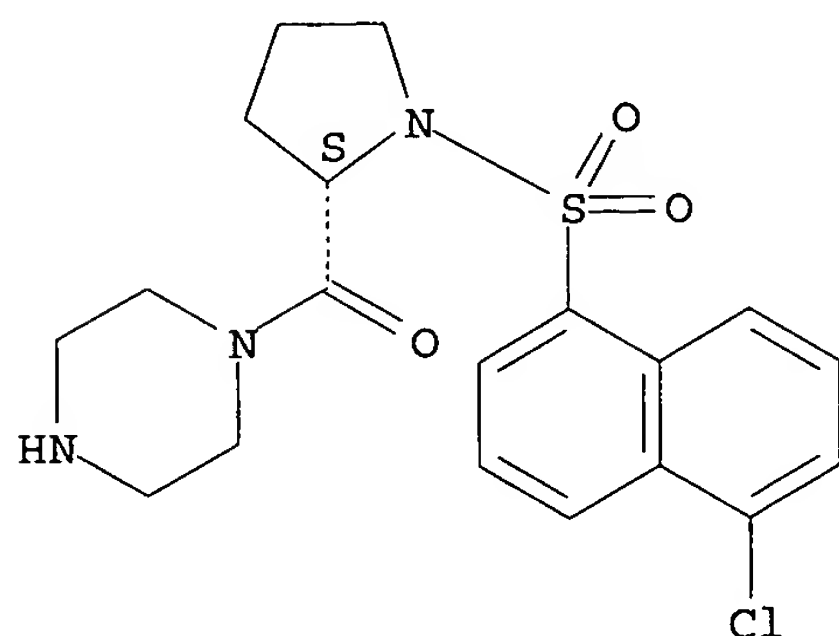
Absolute stereochemistry.



● HCl

RN 149569-33-5 HCAPLUS  
 CN Piperazine, 1-[[1-[(5-chloro-1-naphthalenyl)sulfonyl]-2-pyrrolidinyl]carbonyl]-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

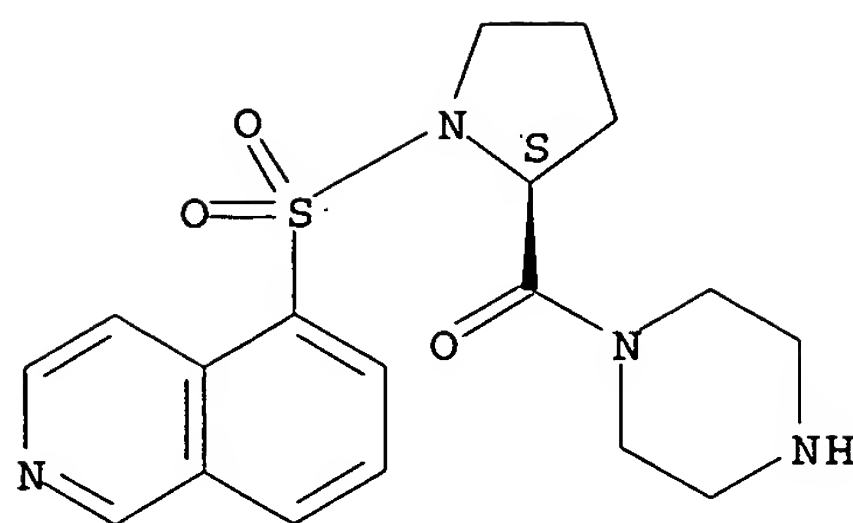
Absolute stereochemistry.



● HCl

RN 149569-39-1 HCAPLUS  
 CN Piperazine, 1-[[1-(5-isoquinolinylsulfonyl)-2-pyrrolidinyl]carbonyl]-, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

IT 149586-38-9P 149586-51-6P

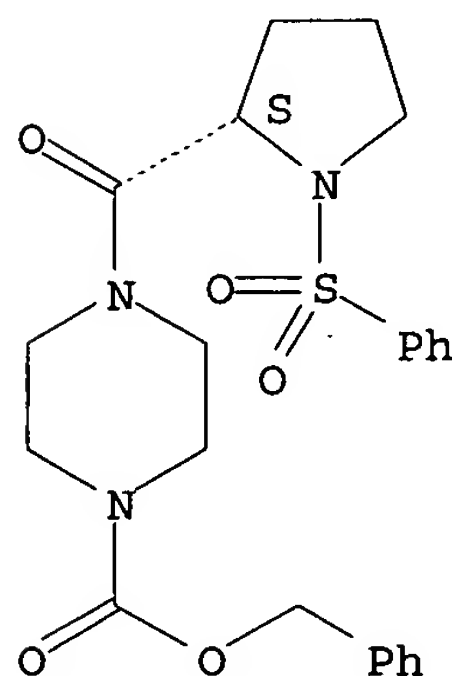
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, as intermediates of calcium-dependent enzyme and phosphokinase inhibitors)

RN 149586-38-9 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[1-(phenylsulfonyl)-2-pyrrolidinyl]carbonyl]-, phenylmethyl ester, (S)- (9CI) (CA INDEX NAME)

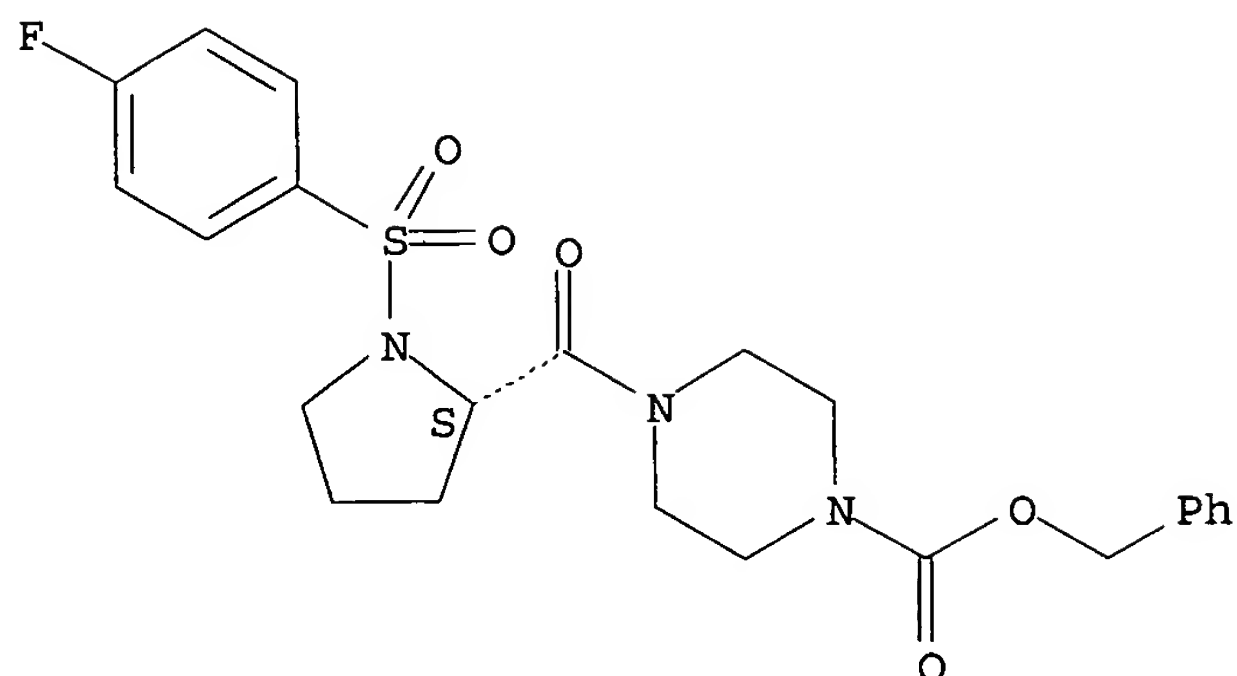
Absolute stereochemistry.



RN 149586-51-6 HCAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[1-[(4-fluorophenyl)sulfonyl]-2-pyrrolidinyl]carbonyl]-, phenylmethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L32 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:553044 HCAPLUS

DOCUMENT NUMBER: 113:153044

TITLE: Process for preparing trans-4-phenyl-L-proline derivatives as intermediates for angiotensin-converting **enzyme** (ACE) **inhibitors**

INVENTOR(S): Kronenthal, David; Kuester, Paula L.; Mueller, Richard H.

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA

SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 61,511, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

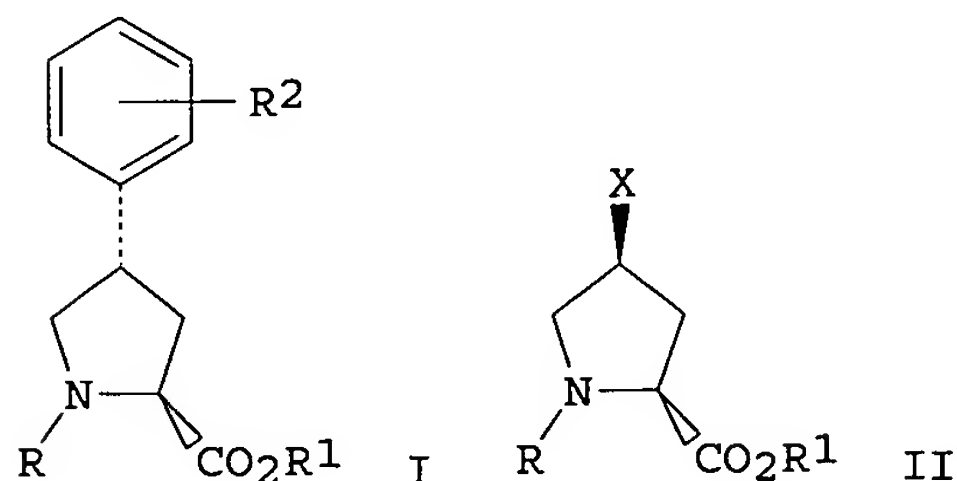
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4912231	A	19900327	US 1988-209165	19880617 <--
CA 1333807	A1	19950103	CA 1988-566007	19880505 <--
GB 2205832	A1	19881221	GB 1988-13659	19880609 <--
GB 2205832	B2	19910717		
FR 2616431	A1	19881216	FR 1988-7841	19880613 <--
FR 2616431	B1	19940812		
JP 01016761	A2	19890120	JP 1988-146690	19880614 <--
JP 08032677	B4	19960329		

PRIORITY APPLN. INFO.: US 1987-61511 B2 19870615

OTHER SOURCE(S): CASREACT 113:153044; MARPAT 113:153044

GI





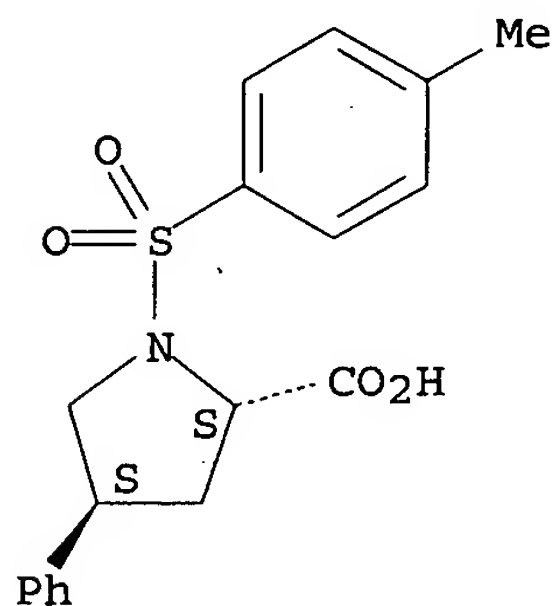
AB Title derivs. I (R = N-protecting group; R1 = H, aryl, alkyl; R2 = H, halo; trans/cis  $\geq$  90:10) are prepared by Friedel-Crafts-type reaction of cis proline derivs. II (X = leaving group) with benzene, a halobenzene, or PhSiMe<sub>3</sub> in the presence of a Lewis acid catalyst at 5-80° under an inert atmosphere. The mol ratio of II to aromatic compound to catalyst is 1:(5-100):(2-10). For example, trans-4-hydroxy-L-proline was subjected to a sequence of N-benzoylation, Me esterification, O-tosylation, saponification, lactonization, methanolysis, O-mesylation, and saponification to give II (R = Bz, R1 = H, X = MeSO<sub>3</sub>). The mesylate was added to excess benzene and AlCl<sub>3</sub>, followed by stirring for 7 h at room temperature, cooling, hydrolysis, and workup (2 crops) to give 81% I (R = Bz, R1 = R2 = H). Preps. of a variety of I and II are described.

IT 120807-08-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as intermediate for ACE inhibitors, via Friedel-Crafts reaction)

RN 120807-08-1 HCAPLUS

CN L-Proline, 1-[(4-methylphenyl)sulfonyl]-4-phenyl-, trans- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L32 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:515737 HCAPLUS

DOCUMENT NUMBER: 111:115737

TITLE: Preparation of trans-4-phenyl-L-proline derivatives as intermediates for ACE (angiotensin-converting enzyme) inhibitors

INVENTOR(S): Kronenthal, David R.; Kuester, Paula L.; Mueller, Richard H.

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA

SOURCE: Ger. Offen., 17 pp.  
 CODEN: GWXXBX

DOCUMENT TYPE: Patent

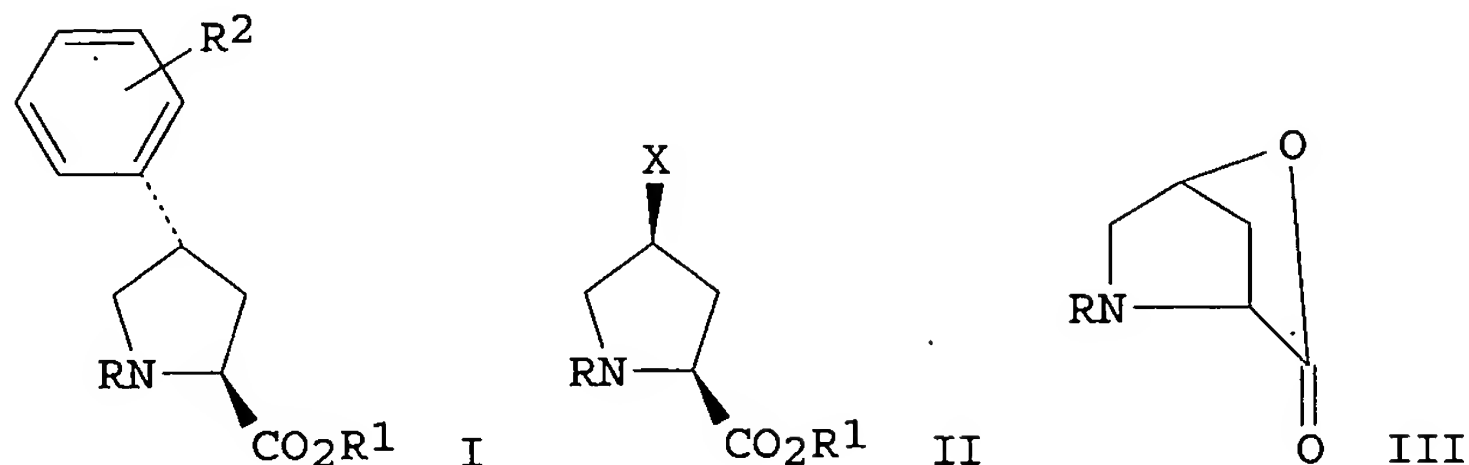
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3820230	A1	19881229	DE 1988-3820230	19880614 <--
DE 3820230	C2	20021107		

CA 1333807	A1	19950103	CA 1988-566007	19880505 <--
GB 2205832	A1	19881221	GB 1988-13659	19880609 <--
GB 2205832	B2	19910717		
FR 2616431	A1	19881216	FR 1988-7841	19880613 <--
FR 2616431	B1	19940812		
JP 01016761	A2	19890120	JP 1988-146690	19880614 <--
JP 08032677	B4	19960329		
PRIORITY APPLN. INFO.:			US 1987-61511	A 19870615
OTHER SOURCE(S):		MARPAT 111:115737		
GI				



AB The title compds. (I; R = protecting group; R<sub>1</sub> = H, aryl, alkyl; R<sub>2</sub> = H, halo), useful as intermediates for ACE inhibitors, were prepared by aromatic nucleophilic substitution of proline derivative II (X = leaving group) or proline lactone III in the presence of Lewis acid catalysts.

1-Benzoyl-allo-hydroxy-L-proline lactone (preparation from trans-4-hydroxy-L-proline given) and AlCl<sub>3</sub> were stirred 2 h at 45° in C<sub>6</sub>H<sub>6</sub> and the mixture was kept for 5 h at room temperature to give 40% I (R = Bz, R<sub>1</sub> = R<sub>2</sub> = H).

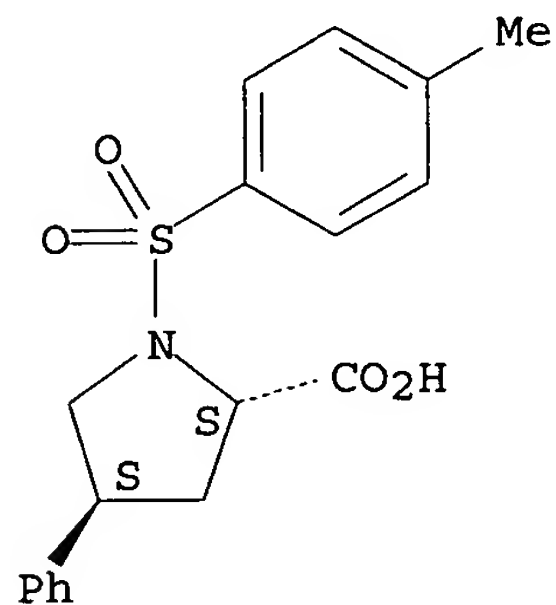
IT 120807-08-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as intermediate for ACE inhibitor)

RN 120807-08-1 HCAPLUS

CN L-Proline, 1-[(4-methylphenyl)sulfonyl]-4-phenyl-, trans- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE COVERS 1907 - 13 May 2005 VOL 142 ISS 21  
FILE LAST UPDATED: 12 May 2005 (20050512/ED)

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L4 STR

Ak~Cy	Ak~O~Ak	G1~Hy~SO2Cy
@10 11	@12 13 14	16 15 8 9

VAR G1=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/10/12

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

GGCAT IS MCY AT 15

DEFAULT ECLEVEL IS LIMITED

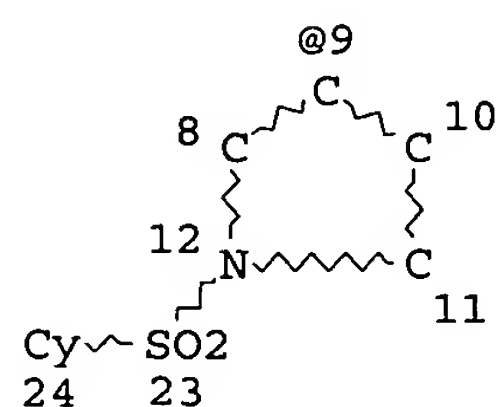
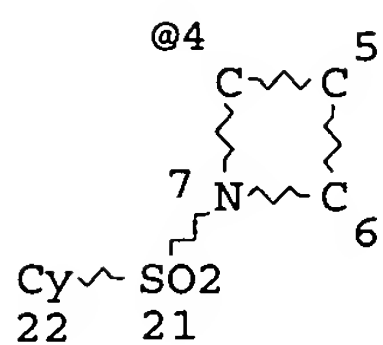
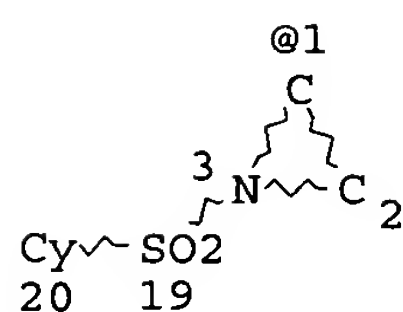
GRAPH ATTRIBUTES:

RSPEC I

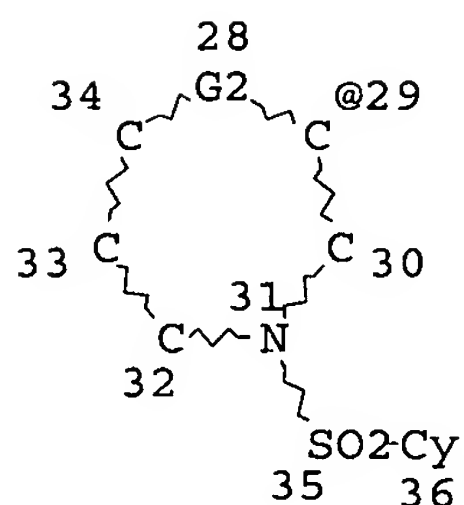
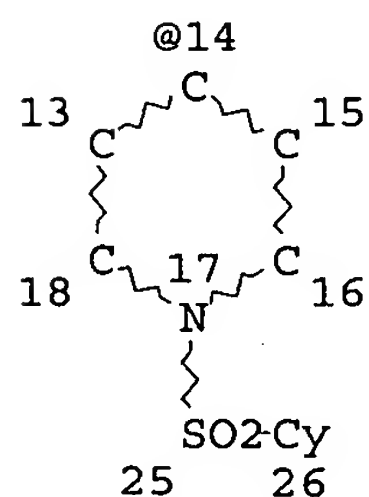
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE

L10 STR



G1 27



VAR G1=1/4/9/14/29

REP G2=(1-5) C

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

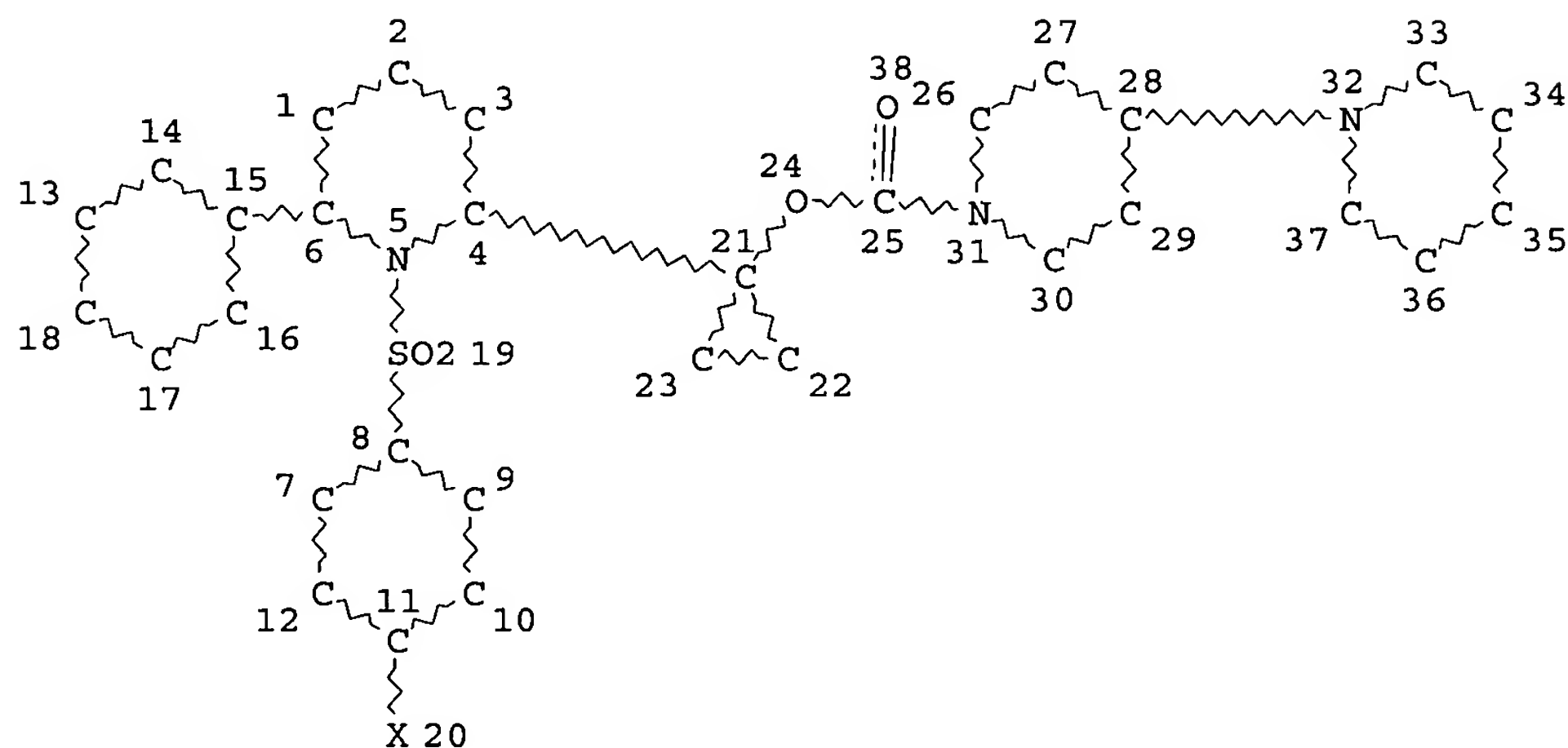
RSPEC I

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L12 25437 SEA FILE=REGISTRY SSS FUL L4 AND L10

L13 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

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L16 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15  
L17 25432 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15  
L18 183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE  
L19 3443 SEA FILE=HCAPLUS ABB=ON PLU=ON L17  
L20 2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?  
L21 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND L20  
L22 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L16  
L23 450 SEA FILE=HCAPLUS ABB=ON PLU=ON L19(L) INHIBIT?  
L24 372 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND PD=<DECEMBER 8, 2003  
L25 301 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND PATENT/DT  
L29 78 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND ENZYME(L) INHIBIT?  
L31 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L25  
L32 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L31 NOT (L16 OR L22)  
L33 13 SEA FILE=HCAPLUS ABB=ON PLU=ON ("PISSARNITSKI DMITRI"/AU OR  
"PISSARNITSKI DMITRI A"/AU) NOT (L16 OR L22 OR L32)

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=> d ibib abs l33 1-13

L33 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:331941 HCAPLUS

TITLE: Optimization of purine based PDE1/PDE5 inhibitors to a potent and selective PDE5 inhibitor for the treatment of male ED

AUTHOR(S): Boyle, Craig D.; Xu, Ruo; Asberom, Theodros; Chackalamannil, Samuel; Clader, John W.; Greenlee, William J.; Guzik, Henry; Hu, Yuequing; Hu, Zhiyong; Lankin, Claire M.; Pissarnitski, Dmitri A.; Stamford, Andrew W.; Wang, Yuguang; Skell, Jeffrey; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Madhu; Wu, Ping; Myers, Joyce; Wang, Peng

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(9), 2365-2369

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In search of a PDE5 inhibitor for erectile dysfunction, an SAR was developed from a PDE1/PDE5 purine series of leads, which had modest PDE5 potency and poor isoenzyme selectivity. A compound (41) with PDE5 inhibition and in vivo activity similar to sildenafil was discovered from this effort. In addition, purine 41 demonstrated superior overall PDE isoenzyme selectivity when compared to the approved PDE5 inhibitors sildenafil, vardenafil, and tadalafil, which may result in a more favorable side-effect profile.

L33 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:226370 HCAPLUS

TITLE: Discovery of a PDE5 inhibitor for the treatment of

male ED

AUTHOR(S): Boyle, Craig D.; Chackalamannil, Samuel; Lankin, Claire M.; Wang, Yuguang; Hu, Zhiyong; Asberom, Theodros; Clader, John W.; Greenlee, William J.; Guzik, Henry; **Pissarnitski, Dmitri**; Stamford, Andrew W.; Xu, Ruo; Skell, Jeffrey; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Mahdu; Wu, Ping; Myers, Joyce; Wang, Peng

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-012. American Chemical Society: Washington, D. C.  
CODEN: 69FGKM

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Using a stepwise approach to improve upon the phys. and pharmacol. properties of a xanthine lead structure, we discovered a PDE5 inhibitor for the treatment of male ED. This compound improves upon the PDE isoenzyme selectivity, enzyme inhibition, and PK profile of the leading drug on the market, sildenafil (Viagra). This paper will summarize the medicinal chemical effort toward the discovery of potent and selective PDE5 inhibitors.

L33 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:153600 HCAPLUS

DOCUMENT NUMBER: 140:350038

TITLE: SAR development of polycyclic guanine derivatives targeted to the discovery of a selective PDE5 inhibitor for treatment of erectile dysfunction

AUTHOR(S): **Pissarnitski, Dmitri A.**; Asberom, Theodros; Boyle, Craig D.; Chackalamannil, Samuel; Chintala, Madhu; Clader, John W.; Greenlee, William J.; Hu, Yueqing; Kurowski, Stanley; Myers, Joyce; Palamanda, Jairam; Stamford, Andrew W.; Vemulapalli, Subbarao; Wang, Yuguang; Wang, Peng; Wu, Ping; Xu, Ruo

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(5), 1291-1294  
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Development of structure-activity relationship of cyclic guanines I lead us to discovery of a potent and selective series of phosphodiesterase 5 inhibitors 52-59 (IC<sub>50</sub>=1.3-11.0 nM, PDE<sub>6/5</sub>=116-600).

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:634975 HCAPLUS

TITLE: Discovery of Sch 444877, a potent, selective and orally active cyclic guanine PDE5 inhibitor

AUTHOR(S): Wang, Yuguang; Chackalamannil, Samuel; Stamford, Andrew; Boyle, Craig D.; Hu, Zhiyong; Lankin, Claire; Clader, John; Xu, Ruo; Asberom, Theodros; **Pissarnitski, Dmitri**; Greenlee, William; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda,

Jairam; Chintala, Mahdu; Wu, Ping; Myers, Joyce; Wang, Peng  
 CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA  
 SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-367. American Chemical Society: Washington, D. C.  
 CODEN: 69EKY9  
 DOCUMENT TYPE: Conference; Meeting Abstract  
 LANGUAGE: English  
 AB Sch 444877 is a tricyclic guanine derived potent inhibitor of human PDE5 isoenzyme with an IC50 value of 1.5 nM. Its PDE6/PDE5 selectivity is about 250-fold. In the dog pelvic nerve stimulation model, Sch 444877 dose-dependently increased cavernosal pressure with an ED100 slightly more potent than sildenafil. It also showed a rapid onset and fast clearance PK profile.

L33 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:396889 HCAPLUS

DOCUMENT NUMBER: 138:401744

TITLE: Preparation of polycyclic guanine derivative phosphodiesterase V inhibitors

INVENTOR(S): Asberom, Theodoros; Clader, John W.; Hu, Yueqing; Pissarnitski, Dmitri A.; Stamford, Andrew W.; Xu, Ruo

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042216	A1	20030522	WO 2002-US35721	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003176413	A1	20030918	US 2002-290011	20021107
EP 1442042	A1	20040804	EP 2002-786685	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005509038	T2	20050407	JP 2003-544052	20021107
PRIORITY APPLN. INFO.:			US 2001-344498P	P 20011109
			WO 2002-US35721	W 20021107
OTHER SOURCE(S):			MARPAT 138:401744	
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*



AB Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y = alkyl, aryl] are prepared For instance, 4-amino-1-benzyl-5-(ethoxycarbonyl)imidazole (preparation given) is treated with ethylisocyanate (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe, reflux, 4 h), subsequently treated with POCl<sub>3</sub> and the product used to alkylate (R)-2-amino-3-phenylpropanol (NMP, 130°, 12 h) which provides II. II is treated with MsCl (Et<sub>3</sub>N), debenzylated (MeOH, NH<sub>4</sub>O<sub>2</sub>CH, Pd(OH)<sub>2</sub>/C, reflux, 3 h), brominated (HOAc, NaOAc, Br<sub>2</sub>), alkylated with 3-chloro-4-methoxybenzyl bromide (DMF, K<sub>2</sub>CO<sub>3</sub>) and treated with NaOEt (DMF/EtOH) to afford III. III has IC<sub>50</sub> < 4.1 nM for PDE V and IC<sub>50</sub> > 300 nM for PDE VI. I are useful for treating sexual dysfunction.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:202642 HCAPLUS

DOCUMENT NUMBER: 138:238193

TITLE: Preparation of polycyclic guanines for therapeutic use as phosphodiesterase V inhibitors

INVENTOR(S): Asberom, Theodoros; Hu, Yueqing; **Pissarnitski, Dmitri A.**; Xu, Ruo; Wang, Yuguang; Chackalamannil, Samuel; Clader, John W.; Stamford, Andrew W.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 179 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

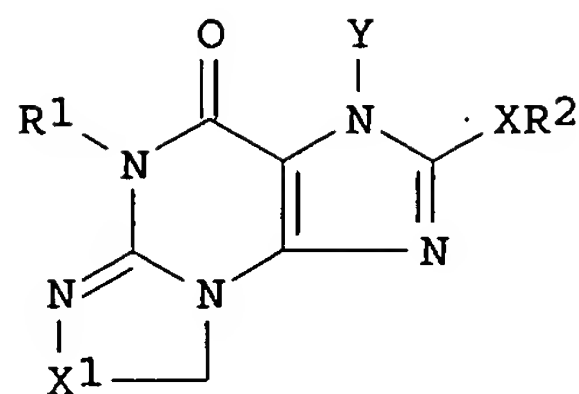
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020724	A1	20030313	WO 2002-US27181	20020826
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2457944	AA	20030313	CA 2002-2457944	20020826
US 2003153587	A1	20030814	US 2002-227778	20020826
EP 1421084	A1	20040526	EP 2002-761506	20020826
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JP 2005502684	T2	20050127	JP 2003-524994	20020826
PRIORITY APPLN. INFO.:			US 2001-315395P	P 20010828
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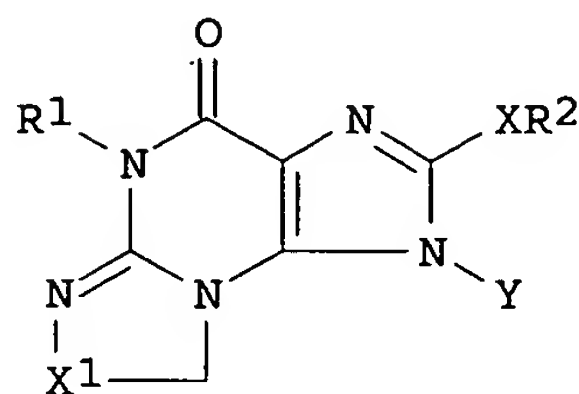
OTHER SOURCE(S): MARPAT 138:238193

GI

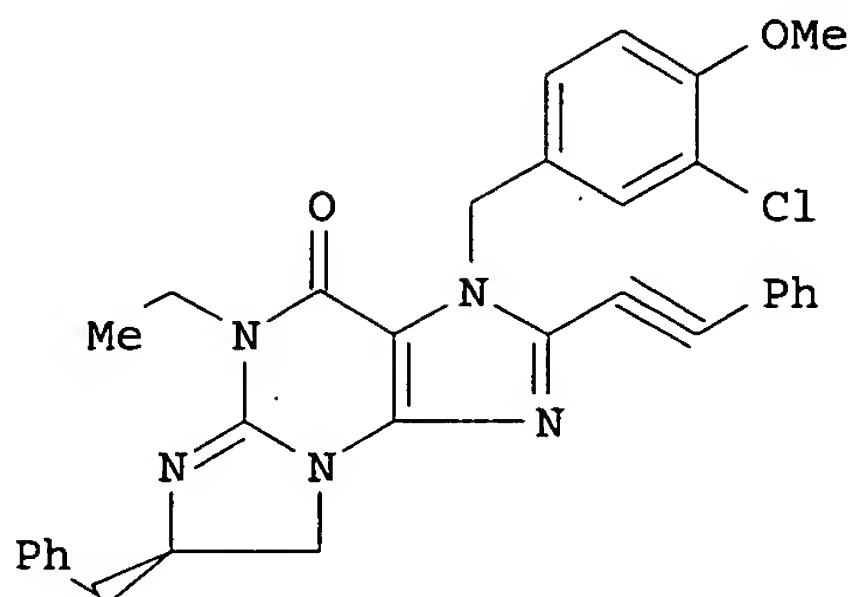




I



II



III

AB Purine cyclic derivs., such as I and II [R1 = H, alkyl, cycloalkyl; R2 = N3, CN, oximino, halo, haloalkyl, cycloalkenyl, heteroaryl, etc.; R3 = H, alkyl, arylalkyl, etc.; X = bond, connecting group, such as O, S, SO, SO2, amino, etc.; X1 = (CH2)2, CHR3, etc.; Y = H, alkyl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase V (PDE5) inhibitors. These polycyclic guanines are useful for treatment of physiol. disorders, wherein the physiol. disorder, symptom or disease is urogenital, such as male erectile dysfunction, peripheral vascular, angina pectoris, restenosis post angioplasty, endarterectomy, stent introduction, cerebral stroke, respiratory tract, allergic associated with atopy, pulmonary hypertension, ischemic heart, impaired glucose tolerance, diabetes, neuropathy, insulin resistance syndrome, hyperglycemia, polycystic ovarian syndrome, glomerular renal insufficiency, nephritis, tubular interstitial, autoimmune, glaucoma, intestinal motility, cachexia, cancer, cognitive impairment or nutcracker esophageal. Thus, polycyclic guanine III was prepared via a multistep synthetic sequence which included cyclization of (R)-2-amino-3-phenyl-1-propanol with 2-chloro-1-ethyl-1,7-dihydro-7-(phenylmethyl)-6H-purin-6-one to form the desired cyclic guanine ring, followed sequentially by removal of the benzyl group using Pd(OH)2/C in MeOH, 8-bromination using Br2 and NaOAc, 7-benylation with 3-chloro-4-methoxybenzyl bromide using K2CO3 in DMF, and finally, alkynylation with phenylacetylene using (PPh3)2PdCl2, CuI and Et3N. The prepared polycyclic guanines were assayed for inhibition of PDE5 activity.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133232 HCAPLUS

DOCUMENT NUMBER: 138:187649

TITLE: Preparation of 1-sulfonyl quinoline derivatives as  $\gamma$ -secretase inhibitors.

INVENTOR(S): Asberom, Theodoros; Guzik, Henry S.; Josien, Hubert B.; Pissarnitski, Dmitri A.

PATENT ASSIGNEE(S): Schering Corporation, USA

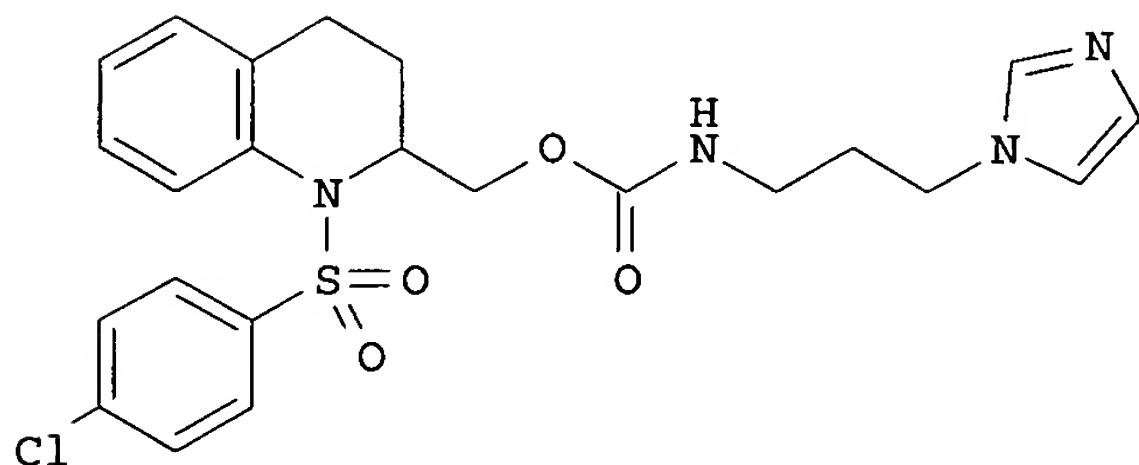
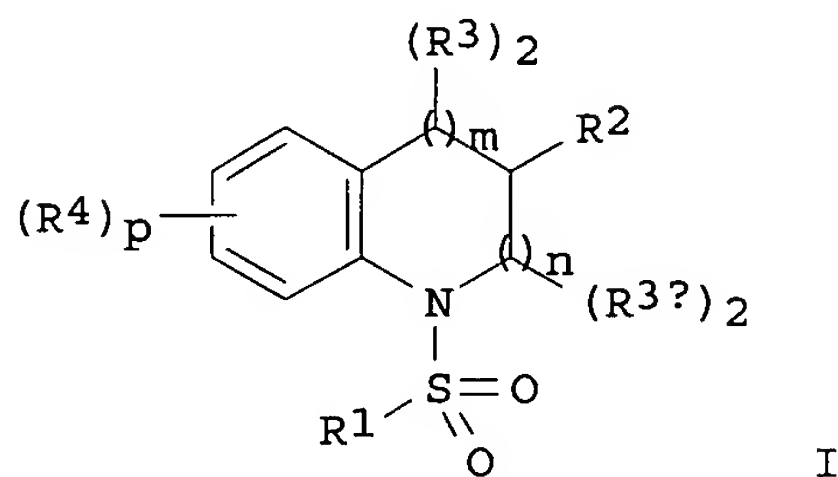
SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014075	A2	20030220	WO 2002-US24323	20020801
WO 2003014075	A3	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2455863	AA	20030220	CA 2002-2455863	20020801
US 2003135044	A1	20030717	US 2002-210829	20020801
US 6683091	B2	20040127		
BR 2002011698	A	20041109	BR 2002-11698	20020801
EP 1492765	A2	20050105	EP 2002-759233	20020801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005504760	T2	20050217	JP 2003-519025	20020801
PRIORITY APPLN. INFO.:				
			US 2001-310013P	P 20010803
			US 2002-355510P	P 20020206
			WO 2002-US24323	W 20020801

OTHER SOURCE(S): MARPAT 138:187649  
 GI



AB Title compds. I [R1 = aryl, heteroaryl; R2 = alkyl, XCOY, etc; R3-3a = H, alkyl; R4 = halo, CF3, OH, alkoxy, etc.; X = O, NH, N-alkyl; Y = amino; m, n = 0-3 such that m + n = 1-4; p = 0-4] are prepared For instance, quinaldic acid is converted to the 2-hydroxymethyl-1,2,3,4-tetrahydroquinoline (MeOH, H2-PtO; MeOH, SOCl2; THF, LAH); this is protected as the TMS-ether derivative and sulfonylated (CH2Cl2, Et3N, TMSCl; Et3N, 4-ClC6H4SO2Cl). This intermediate is desilylated (MeOH, K2CO3), converted to the 4-nitrophenylcarbonate and treated with 1-(3-aminopropyl)imidazole to give II. Selected compds. of the invention have IC50 in the range of about 0.030 to 24.45  $\mu$ M for  $\gamma$ -secretase. I are useful for the treatment of Alzheimer's Disease.

L33 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133040 HCAPLUS

DOCUMENT NUMBER: 138:170082

TITLE: Preparation of piperidinylsulfonamides as  $\gamma$ -secretase inhibitors

INVENTOR(S): Josien, Hubert B.; Clader, John W.; Asberom, Theodros; Pissarnitski, Dmitri A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

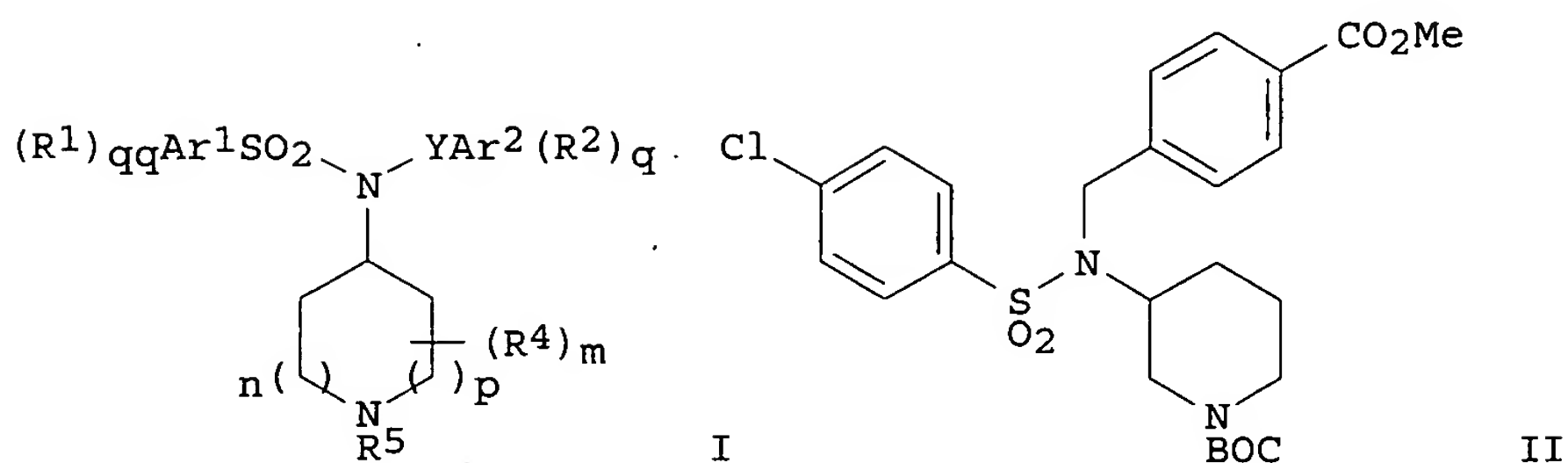
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013527	A1	20030220	WO 2002-US24293	20020801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2455861	AA	20030220	CA 2002-2455861	20020801
US 2003216380	A1	20031120	US 2002-210803	20020801
EP 1411944	A1	20040428	EP 2002-761207	20020801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005504042	T2	20050210	JP 2003-518536	20020801
PRIORITY APPLN. INFO.:			US 2001-310068P	P 20010803
			WO 2002-US24293	W 20020801
OTHER SOURCE(S):		MARPAT 138:170082		
GI				



AB Title compds. [I; Ar1, Ar2 = aryl, heteroaryl; Y = bond, [C(R3)2]1-3; R1 = halo, CF3, OCF3, cyano, amino, alkyl, alkylaminocarbonyl, (substituted) aryl, heteroaryl, etc.; R2 = alkyl, halo, CF3, OCF3, cyano, NO2, amino, OH, alkoxycarbonyl, alkylaminocarbonyl, alkoxy, aryloxy, etc.; R3 = H, alkyl; R4 = alkyl, OH, alkoxy; R5 = H, alkyl, aryl, heteroaryl, alkoxyalkylene, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, alkylsulfonyl, alkylaminosulfonyl, etc.; m, n, p, q, qq = 0-3], were prepared. Thus, 3-amino-1-tert-butoxycarbonylpiperidine, Me 4-formylbenzoate, and 4 Å mol. sieves were stirred together in MeOH overnight; NaBH4 was added followed by 3 h stirring to give 85% benzylpiperidinylamine derivative. This was stirred 2 days with 4-ClC6H4SO2Cl and Et3N in CH2Cl2 to give 77% title compound (II). I inhibited  $\gamma$ -secretase with IC50 = 0.028-69.550  $\mu$ M.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:767305 HCAPLUS

DOCUMENT NUMBER: 138:331192

TITLE: Design and synthesis of xanthine analogues as potent and selective PDE5 inhibitors

AUTHOR(S): Wang, Yuguang; Chackalamannil, Samuel; Hu, Zhiyong; Boyle, Craig D.; Lankin, Claire M.; Xia, Yan; Xu, Ruo; Asberom, Theodros; Pissarnitski, Dmitri; Stamford, Andrew W.; Greenlee, William J.; Skell, Jeffrey; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Madhu; Wu, Ping; Myers, Joyce; Wang, Peng

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(21), 3149-3152

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have discovered potent and selective xanthine PDE5 inhibitors. One compound (PDE5 IC50=0.6 nM, PDE6/PDE5=101) demonstrated similar functional efficacy and pharmacokinetic profile to sildenafil (PDE5 IC50=3.5 nM, PDE6/PDE5=7).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

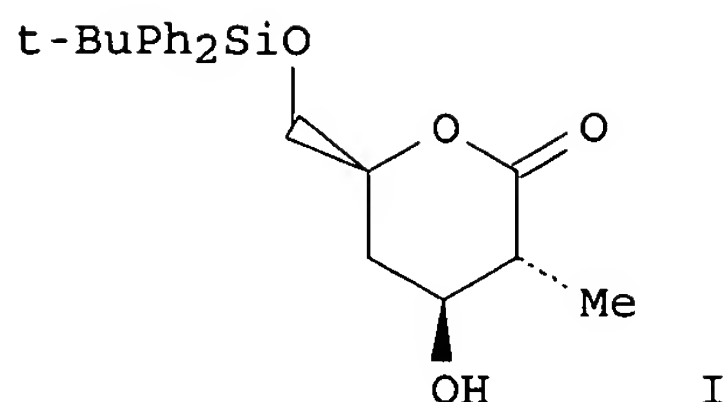
ACCESSION NUMBER: 1999:815366 HCAPLUS

DOCUMENT NUMBER: 132:222730

TITLE: Stereocontrolled Elaboration of Natural  
 (-)-Polycavernoside A, a Powerfully Toxic Metabolite  
 of the Red Alga Polycavernosa tsudai  
 AUTHOR(S): Paquette, Leo A.; Barriault, Louis; **Pissarnitski,**  
**Dmitri**; Johnston, Jeffrey N.  
 CORPORATE SOURCE: Evans Chemical Laboratories, The Ohio State  
 University, Columbus, OH, 43210, USA  
 SOURCE: Journal of the American Chemical Society (2000),  
 122(4), 619-631  
 CODEN: JACSAT; ISSN: 0002-7863  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 132:222730  
 AB A stereoselective total synthesis of natural levorotatory polycavernoside  
 A has been achieved. Initial investigations produced the properly  
 activated disaccharide unit via the conjoining of building blocks  
 originating from L-fucose and D-xylose.  
 REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1999:283406 HCAPLUS  
 DOCUMENT NUMBER: 130:338300  
 TITLE: An approach to the enantioselective synthesis of  
 polycavernoside a: investigation of sulfur-stabilized  
 carbanion chemistry for union of the southern and  
 northern fragments of the aglycone  
 AUTHOR(S): **Pissarnitski, Dmitri**  
 CORPORATE SOURCE: Ohio State Univ., Columbus, OH, USA  
 SOURCE: (1998) 235 pp. Avail.: UMI, Order No. DA9911250  
 From: Diss. Abstr. Int., B 1999, 59(10), 5369  
 DOCUMENT TYPE: Dissertation  
 LANGUAGE: English  
 AB Unavailable

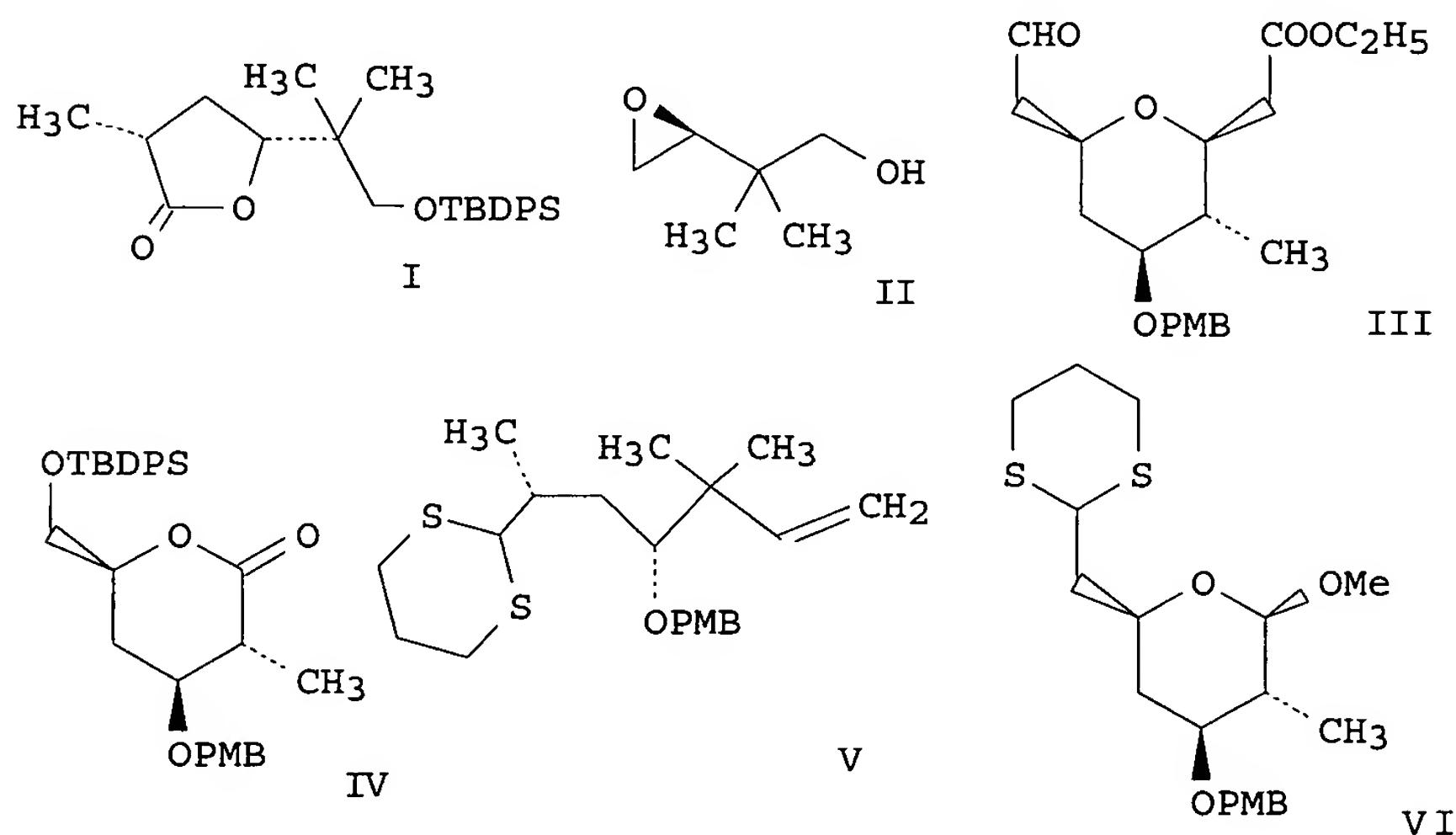
L33. ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1999:257527 HCAPLUS  
 DOCUMENT NUMBER: 130:338306  
 TITLE: A Convergent Total Synthesis of the Macrolactone  
 Disaccharide Toxin (-)-Polycavernoside A  
 AUTHOR(S): Paquette, Leo A.; Barriault, Louis; **Pissarnitski,**  
**Dmitri**  
 CORPORATE SOURCE: Evans Chemical Laboratories, The Ohio State  
 University, Columbus, OH, 43210, USA  
 SOURCE: Journal of the American Chemical Society (1999),  
 121(18), 4542-4543  
 CODEN: JACSAT; ISSN: 0002-7863  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB Title (-)-polycavernoside A was prepared from lactone I via coupling with disaccharide.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1998:632427 HCAPLUS  
 DOCUMENT NUMBER: 129:330944  
 TITLE: A Modular Enantioselective Approach to Construction of the Macrolactone Core of Polycavernoside A  
 AUTHOR(S): Paquette, Leo A.; Pissarnitski, Dmitri; Barriault, Louis  
 CORPORATE SOURCE: Evans Chemical Laboratories, The Ohio State University, Columbus, OH, 43210, USA  
 SOURCE: Journal of Organic Chemistry (1998), 63(21), 7389-7398  
 CODEN: JOCEAH; ISSN: 0022-3263  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB A program directed toward a total synthesis of polycavernoside A is described. The synthesis of five building blocks is detailed. The first

of two electrophilic units, the lactone (I), was prepared in four steps from the known enantiomerically pure oxirane (II). Pyranaldehyde (III) was elaborated in turn from L-malic acid via (IV). While the route to (V) involved I as a starting material, dithiane (VI) was obtained in a straightforward manner from IV as well. The merging of the chiral sectors could not be accomplished by way of the lithiated dithianyl anions, presumably as a consequence of their heightened basicity. The strategic incorporation of the trienyl sector was accomplished, although no attempt was made to control the diastereoselectivity of the process.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L4 STR

Ak~Cy	Ak~O~Ak	G1~Hy~SO2Cy
@10 11	@12 13 14	16 15 8 9

VAR G1=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/10/12

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

GGCAT IS MCY AT 15

DEFAULT ECLEVEL IS LIMITED

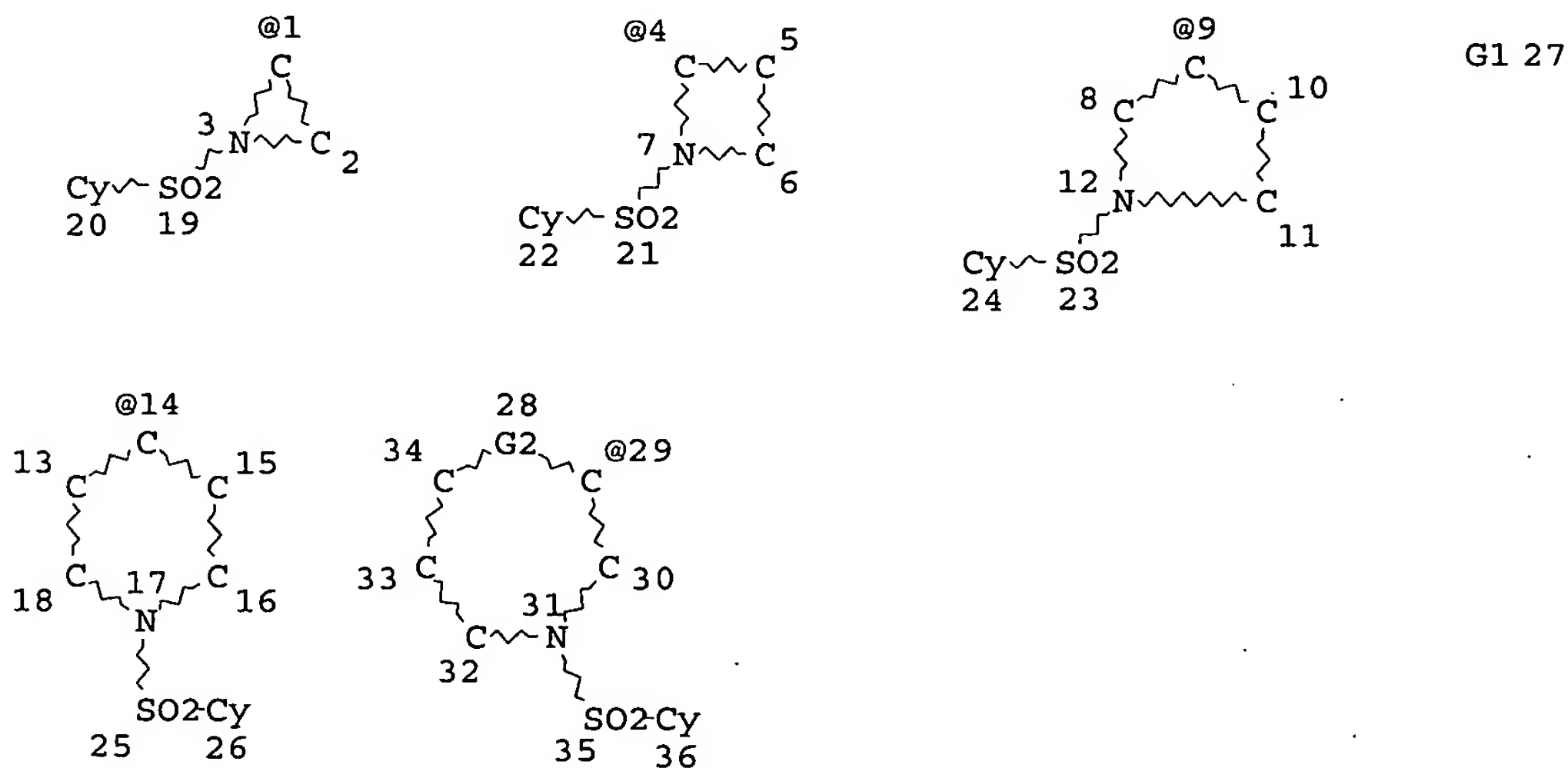
GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE

L10 STR



VAR G1=1/4/9/14/29

REP G2=(1-5) C

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED



GRAPH ATTRIBUTES:

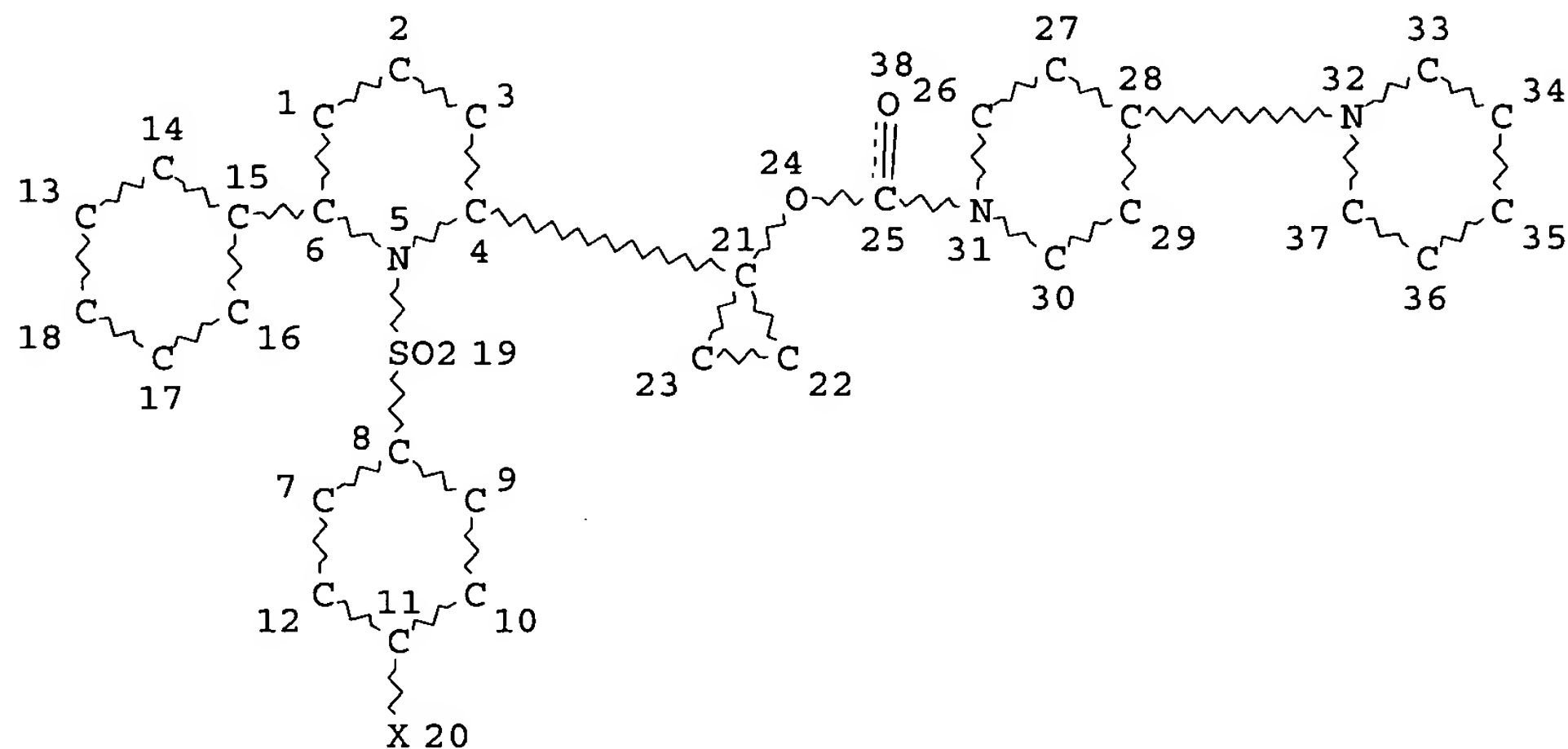
RSPEC I

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L12 25437 SEA FILE=REGISTRY SSS FUL L4 AND L10

L13 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

L15 5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13

L16 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15

L17 25432 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15

L18 183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE

L19 3443 SEA FILE=HCAPLUS ABB=ON PLU=ON L17

L20 2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?

L21 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND L20

L22 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L16

L23 450 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 (L) INHIBIT?

L24 372 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND PD=<DECEMBER 8, 2003

L25 301 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND PATENT/DT

L29 78 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND ENZYME(L) INHIBIT?

L31 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L25

L32 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L31 NOT (L16 OR L22)

L34 40 SEA FILE=HCAPLUS ABB=ON PLU=ON ("JOSIEN H"/AU OR "JOSIEN H B"/AU OR "JOSIEN HUBERT"/AU OR "JOSIEN HUBERT B"/AU) NOT (L16 OR L22 OR L32)

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=> d ibib abs 1-40



L34 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:15936 HCAPLUS

DOCUMENT NUMBER: 142:114104

TITLE: A preparation of pyrazine derivatives, useful as MCH antagonists

INVENTOR(S): Palani, Anandan; Shapiro, Sherry A.; Josien, Hubert B.; Bara, Thomas A.; Clader, John W.; Pushpavanam, Pradeep B.; Li, Shengjian; McBriar, Mark D.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 34 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005004121	A1	20050106	US 2004-878788	20040628
WO 2005005419	A1	20050120	WO 2004-US20763	20040628
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2003-483619P P 20030630

OTHER SOURCE(S): MARPAT 142:114104

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to a preparation of pyrazine derivs. of formula I [wherein: Ar is aryl; R1 is C(O)aryl, O-alkyl, halogen, or heteroaryl, etc.; R2 and R3 are independently selected from H, alkyl, or (hetero)aryl; R4 is H or alkyl; R5 is (cyclo)alkyl or aryl], useful as melanin-concentrating hormone (MCH) antagonists (antiobesity agents). For instance, pyrazine derivative II (10nM < Ki < 15nM) was prepared via amidation of 3-propoxythiophene-2-carboxylic acid by pyrazinylpiperidine derivative III with a yield of 54%.

L34 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:239373 HCAPLUS

DOCUMENT NUMBER: 141:1035

TITLE: Chronic Treatment with the  $\gamma$ -Secretase Inhibitor LY-411575 Inhibits  $\beta$ -Amyloid Peptide Production and Alters Lymphopoiesis and Intestinal Cell Differentiation

AUTHOR(S): Wong, Gwendolyn T.; Manfra, Denise; Poulet, Frederique M.; Zhang, Qi; Josien, Hubert; Bara, Thomas;

Engstrom, Laura; Pinzon-Ortiz, Maria; Fine, Jay S.;  
Lee, Hu-Jung J.; Zhang, Lili; Higgins, Guy A.; Parker,  
Eric M.

CORPORATE SOURCE: Chemical Research, Immunology, Departments of Central  
Nervous System Research, Schering-Plough Research  
Institute, Kenilworth, NJ, 07033, USA

SOURCE: Journal of Biological Chemistry (2004), 279(13),  
12876-12882

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular  
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibition of  $\gamma$ -secretase, one of the enzymes responsible for the  
cleavage of the amyloid precursor protein (APP) to produce the pathogenic  
 $\beta$ -amyloid (A $\beta$ ) peptides, is an attractive approach to the  
treatment of Alzheimer disease. In addition to APP, however, several other  
 $\gamma$ -secretase substrates have been identified (e.g. Notch), and  
altered processing of these substrates by  $\gamma$ -secretase inhibitors  
could lead to unintended biol. consequences. To study the in vivo  
consequences of  $\gamma$ -secretase inhibition, the  $\gamma$ -secretase  
inhibitor LY-411575 was administered to C57BL/6 and TgCRND8 APP transgenic  
mice for 15 days. Although most tissues were unaffected, doses of  
LY-411575 that inhibited A $\beta$  production had marked effects on lymphocyte  
development and on the intestine. LY-411575 decreased overall thymic  
cellularity and impaired intrathymic differentiation at the  
CD4-CD8-CD44+CD25+ precursor stage. No effects on peripheral T cell  
populations were noted following LY-411575 treatment, but evidence for the  
altered maturation of peripheral B cells was observed. In the intestine,  
LY-411575 treatment increased goblet cell number and drastically altered  
tissue morphol. These effects of LY-411575 were not seen in mice that  
were administered LY-D, a diastereoisomer of LY-411575, which is a very  
weak  $\gamma$ -secretase inhibitor. These studies show that inhibition of  
 $\gamma$ -secretase has the expected benefit of reducing A $\beta$  in a murine  
model of Alzheimer disease but has potentially undesirable biol. effects  
as well, most likely because of the inhibition of Notch processing.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133232 HCAPLUS

DOCUMENT NUMBER: 138:187649

TITLE: Preparation of 1-sulfonyl quinoline derivatives as  
 $\gamma$ -secretase inhibitors

INVENTOR(S): Asberom, Theodros; Guzik, Henry S.; Josien,  
Hubert B.; Pissarnitski, Dmitri A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

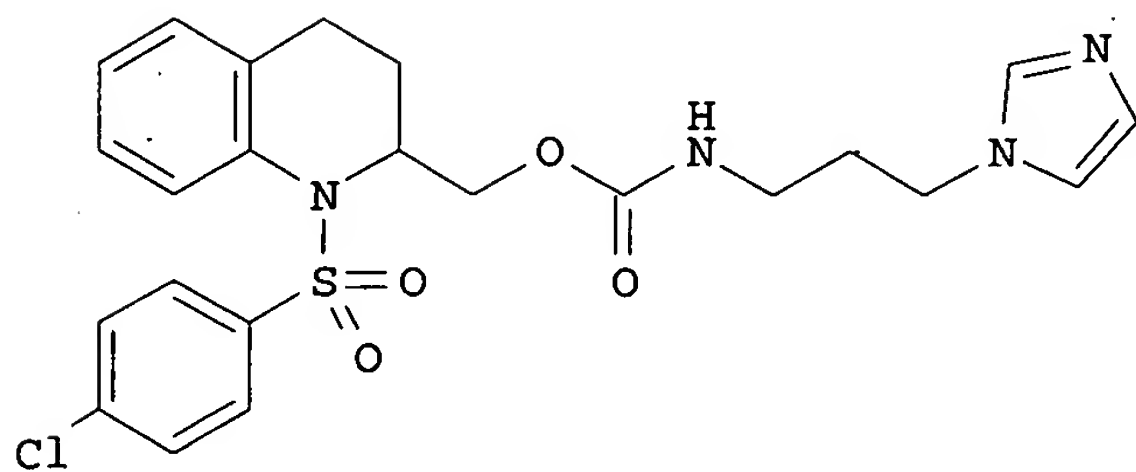
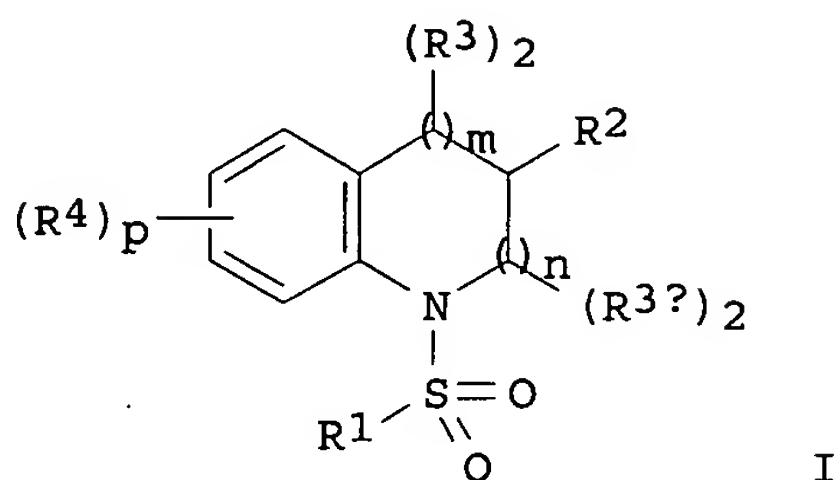
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003014075	A2	20030220	WO 2002-US24323	20020801
WO 2003014075	A3	20040930		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,			
	CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU,			

Ward 10\_663042-inventor search

ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 CA 2455863 AA 20030220 CA 2002-2455863 20020801  
 US 2003135044 A1 20030717 US 2002-210829 20020801  
 US 6683091 B2 20040127  
 BR 2002011698 A 20041109 BR 2002-11698 20020801  
 EP 1492765 A2 20050105 EP 2002-759233 20020801  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
 JP 2005504760 T2 20050217 JP 2003-519025 20020801  
 PRIORITY APPLN. INFO.: US 2001-310013P P 20010803  
 US 2002-355510P P 20020206  
 WO 2002-US24323 W 20020801  
 OTHER SOURCE(S): MARPAT 138:187649  
 GI



AB Title compds. I [R1 = aryl, heteroaryl; R2 = alkyl, XCOY, etc; R3-3a = H, alkyl; R4 = halo, CF3, OH, alkoxy, etc.; X = O, NH, N-alkyl; Y = amino; m, n = 0-3 such that m + n = 1-4; p = 0-4] are prepared For instance, quinaldic acid is converted to the 2-hydroxymethyl-1,2,3,4-tetrahydroquinoline (MeOH, H2-PtO; MeOH, SOCl2; THF, LAH); this is protected as the TMS-ether derivative and sulfonylated (CH2Cl2, Et3N, TMSCl; Et3N, 4-ClC6H4SO2Cl). This intermediate is desilylated (MeOH, K2CO3), converted to the 4-nitrophenylcarbonate and treated with 1-(3-aminopropyl)imidazole to give II. Selected compds. of the invention have IC50 in the range of about 0.030 to 24.45  $\mu$ M for

$\gamma$ -secretase. I are useful for the treatment of Alzheimer's Disease.

L34 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133040 HCAPLUS

DOCUMENT NUMBER: 138:170082

TITLE: Preparation of piperidinylsulfonamides as  $\gamma$ -secretase inhibitors

INVENTOR(S): Josien, Hubert B.; Clader, John W.; Asberom, Theodros; Pissarnitski, Dmitri A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

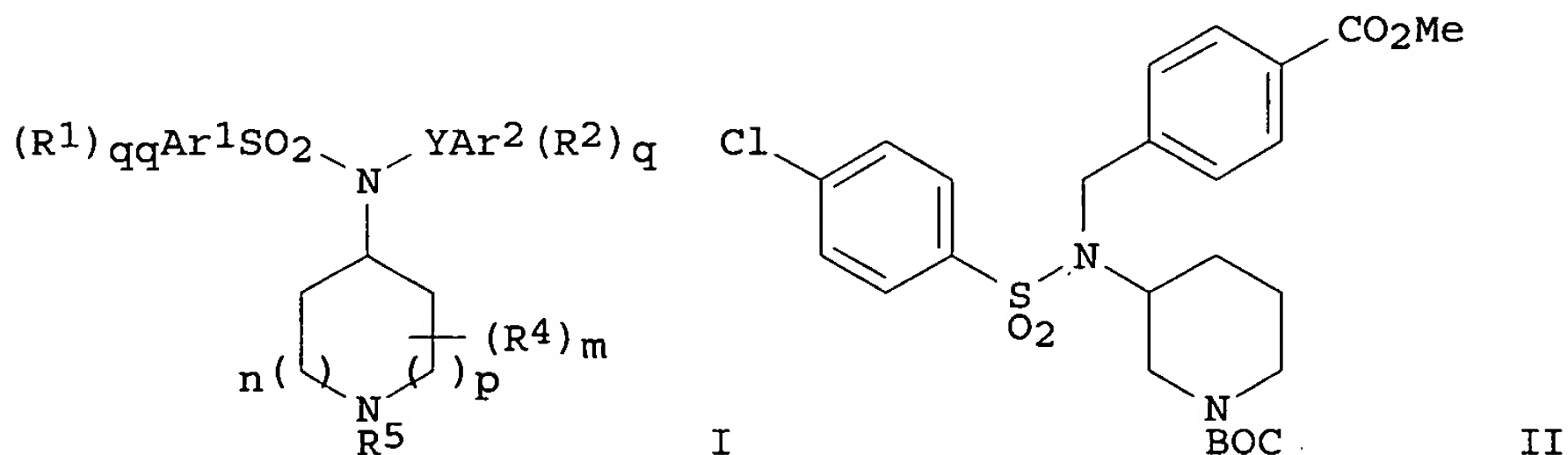
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013527	A1	20030220	WO 2002-US24293	20020801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2455861	AA	20030220	CA 2002-2455861	20020801
US 2003216380	A1	20031120	US 2002-210803	20020801
EP 1411944	A1	20040428	EP 2002-761207	20020801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005504042	T2	20050210	JP 2003-518536	20020801
PRIORITY APPLN. INFO.:			US 2001-310068P	P 20010803
			WO 2002-US24293	W 20020801
OTHER SOURCE(S):			MARPAT 138:170082	
GI				



AB Title compds. [I; Ar1, Ar2 = aryl, heteroaryl; Y = bond, [C(R3)2]1-3; R1 = halo, CF3, OCF3, cyano, amino, alkyl, alkylaminocarbonyl, (substituted) aryl, heteroaryl, etc.; R2 = alkyl, halo, CF3, OCF3, cyano, NO2, amino, OH, alkoxy, alkoxy, alkoxy, aryloxy, etc.; R3 = H, alkyl; R4 = alkyl, OH, alkoxy; R5 = H, alkyl, aryl, heteroaryl,

alkoxyalkylene, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, alkylsulfonyl, alkylaminosulfonyl, etc.; m, n, p, q, qq = 0-3], were prepared. Thus, 3-amino-1-tert-butoxycarbonylpiperidine, Me 4-formylbenzoate, and 4 Å mol. sieves were stirred together in MeOH overnight; NaBH<sub>4</sub> was added followed by 3 h stirring to give 85% benzylpiperidinylamine derivative. This was stirred 2 days with 4-ClC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl and Et<sub>3</sub>N in CH<sub>2</sub>Cl<sub>2</sub> to give 77% title compound (II). I inhibited  $\gamma$ -secretase with IC<sub>50</sub> = 0.028-69.550  $\mu$ M.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:76254 HCAPLUS

DOCUMENT NUMBER: 139:46165

TITLE: Recent advances in the development of  $\gamma$ -secretase inhibitors

AUTHOR(S): Josien, Hubert

CORPORATE SOURCE: CV and CNS Medicinal Chemistry Department, Schering-Plough Research Institute, Kenilworth, NJ, 07033-1300, USA

SOURCE: Current Opinion in Drug Discovery & Development (2002), 5(4), 513-525

CODEN: CODDDFF; ISSN: 1367-6733

PUBLISHER: PharmaPress Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Alzheimer's disease is a neurodegenerative disorder that exerts a huge psychol. and social toll in modern societies. The current hypothesis for the cause of this illness is that it is the result of aberrant production of  $\beta$ -amyloid (A $\beta$ ) and plaque deposition in the brain of affected individuals. New therapeutic interventions seek to stop or even reverse the course of the disease by inhibiting this aggregation or reducing A $\beta$  formation. The use of inhibitors of  $\gamma$ -secretase, a key enzyme in the production of A $\beta$ , is currently undergoing preclin. and clin. evaluation. Small mol. inhibitors which demonstrate efficacy in reducing A $\beta$  burden in mice have thus been recently discovered. This review summarizes the development of such inhibitors in light of the current understanding of the function of  $\gamma$ -secretase. It also provides an evaluation of the therapeutic potential for this class of compds. with the recent discovery of other biochem. pathways associated with  $\gamma$ -secretase, such as Notch signaling.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:754356 HCAPLUS

DOCUMENT NUMBER: 137:279095

TITLE: Preparation of N-[biaryl(piperidinyl)ethyl]-N'-arylureas and analogs as melanin-concentrating hormone receptor antagonists

INVENTOR(S): Clader, John W.; Josien, Hubert B.; Palani, Anandan; Chan, Tin-Yau

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 129 pp.

CODEN: PIXXD2

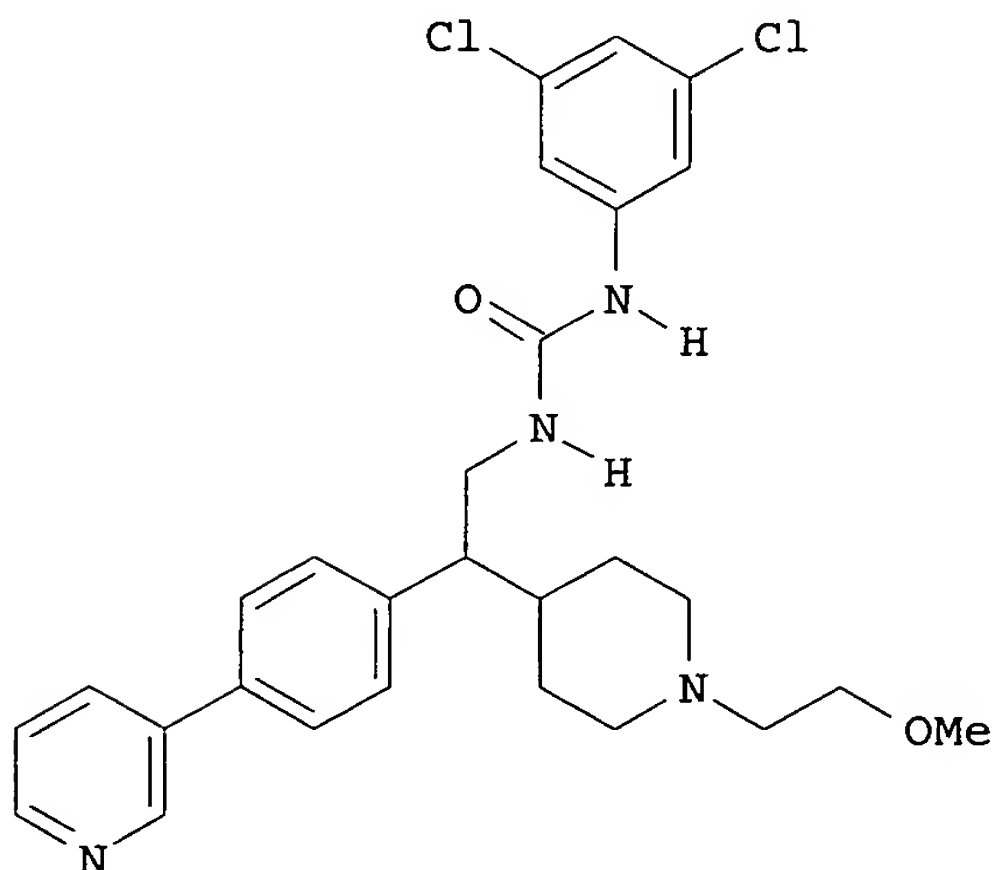
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076947	A1	20021003	WO 2002-US8338	20020320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003105094	A1	20030605	US 2002-100840	20020319
CA 2441239	AA	20021003	CA 2002-2441239	20020320
EP 1370528	A1	20031217	EP 2002-709850	20020320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002008150	A	20040302	BR 2002-8150	20020320
JP 2004532835	T2	20041028	JP 2002-576208	20020320
NO 2003004169	A	20031118	NO 2003-4169	20030919
PRIORITY APPLN. INFO.:			US 2001-277584P	P 20010321
			WO 2002-US8338	W 20020320
OTHER SOURCE(S):			MARPAT 137:279095	
GI				



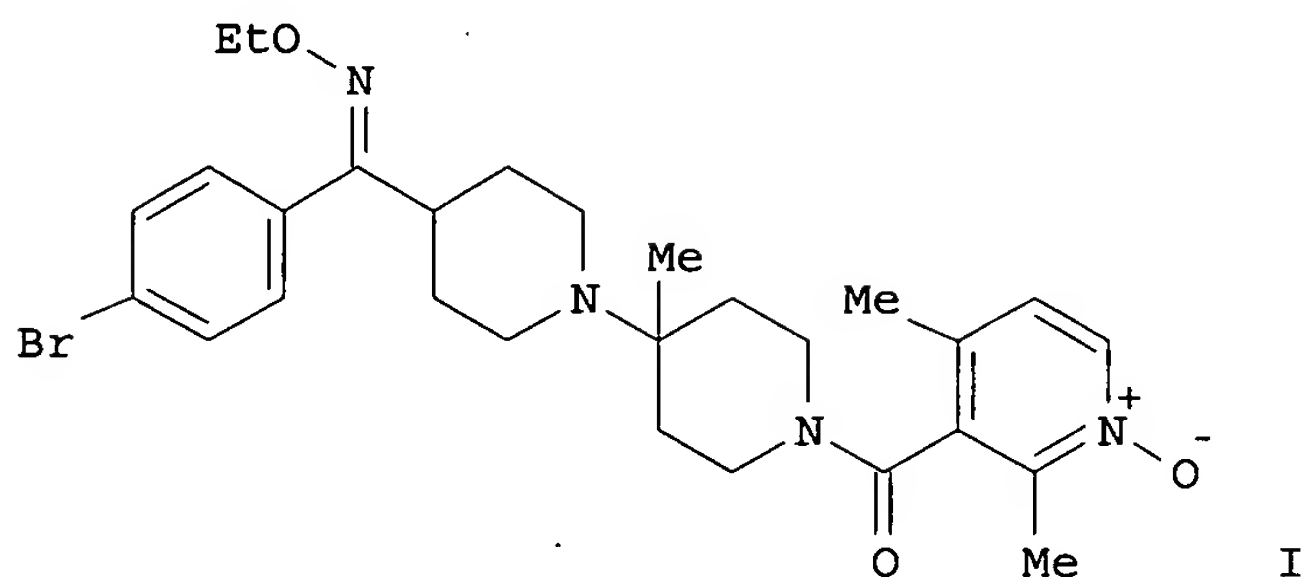
II

AB Title compds., e.g., RZCH(Z1R1)CH2Z2CONHR2 (Z = piperidine-1,4-diyl, Z1 = 1,4-phenylene) [I; R = H, (cyclo)alkyl, alkylsulfonyl, etc.; R1 = (un)substituted Ph or 3-pyridinyl; R2 = halophenyl, (un)substituted pyridinyl, etc.; Z2 = O or NH] were prepared. Thus, BocZCH(Z1Br)CH2OH (preparation given) was aminated and the product condensed with 3,5-Cl2C6H3NCO to give BocZCH(Z2Br)CH2NHCONHC6H3Cl3-3,5 which was converted in 3 steps to title compound II. Data for biol. activity of title compds. were given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



DOCUMENT NUMBER: 137:47089  
 TITLE: Synthesis, SAR, and Biological Evaluation of Oximino-Piperidino-Piperidine Amides. 1. Orally Bioavailable CCR5 Receptor Antagonists with Potent Anti-HIV Activity  
 AUTHOR(S): Palani, Anandan; Shapiro, Sherry; Josien, Hubert; Bara, Thomas; Clader, John W.; Greenlee, William J.; Cox, Kathleen; Strizki, Julie M.; Baroudy, Bahige M.  
 CORPORATE SOURCE: Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA  
 SOURCE: Journal of Medicinal Chemistry (2002), 45(14), 3143-3160  
 CODEN: JMCMAR; ISSN: 0022-2623  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 137:47089  
 GI



AB The discovery of 4-[(Z)-(4-bromophenyl)(ethoxyimino)methyl]-1'-[(2,4-dimethyl-3-pyridinyl)carbonyl]-4'-methyl-1,4'-bipiperidine N-oxide (I; SCH 351125), an orally bioavailable human CCR5 antagonist for the treatment of HIV-1 infection, has been reported. The discovery of I from initial lead compds. is discussed as well as synthesis and SAR studies directed toward optimization of substitution at the Ph, oxime, and right-hand side amide groups in the oximino-piperidino-piperidine series. Substitutions (4-Br, 4-F3C, 4-F3CO, 4-MeSO2, and 4-Cl) at the Ph group are well-tolerated, and small alkyl substitutions (Me, Et, Pr, i-Pr, and cyclopropylmethyl) at the oxime moiety are preferred for CCR5 antagonism. The 2,6-dimethylnicotinamide N-oxide moiety is the optimal choice for the right-hand side. Several compds. in this series, including I, exhibited excellent antiviral activity in vitro. I, which has a favorable pharmacokinetic profile in rodents and primates, excellent oral bioavailability, and potent antiviral activity against a wide range of primary HIV-1 isolates, is a potentially promising new candidate for treatment of HIV-1 infection.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:385004 HCAPLUS  
 DOCUMENT NUMBER: 136:386137

TITLE: Preparation of piperidinylpiperazines as CCR5 chemokine receptor antagonists.

INVENTOR(S): Baroudy, Bahige M.; Clader, John W.; Josien, Hubert B.; McCombie, Stuart W.; McKittrick, Brian A.; Miller, Michael W.; Neustadt, Bernard R.; Palani, Anandan; Smith, Elizabeth M.; Steensma, Ruofu; Tagat, Jayaram R.; Vice, Susan F.; Gilbert, Eric; Labroli, Marc A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S., 72 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

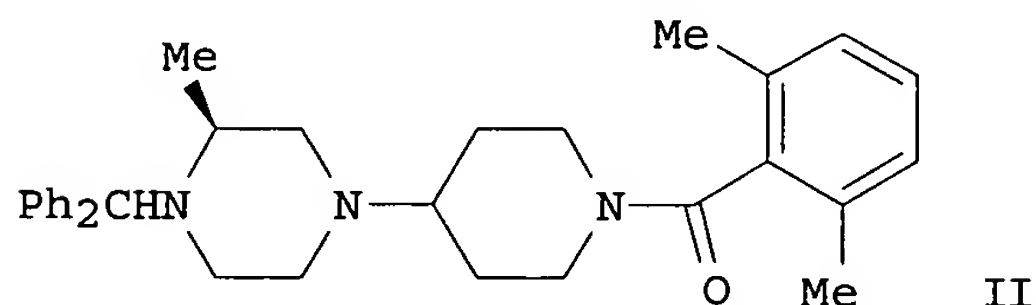
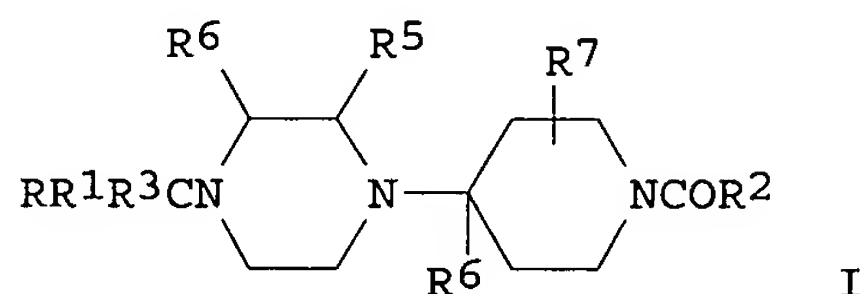
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6391865	B1	20020521	US 2000-562814	20000501
US 2003069252	A1	20030410	US 2002-61011	20020130
US 6689765	B2	20040210		
US 2004067961	A1	20040408	US 2003-668862	20030923
PRIORITY APPLN. INFO.:			US 1999-132509P	P 19990504
			US 2000-562814	A3 20000501
			US 2002-61011	A3 20020130

OTHER SOURCE(S): MARPAT 136:386137

GI



AB Title compds. [I; R = (substituted) Ph, pyridyl, thienyl, naphthyl; R1 = H, alkyl; R2 = (substituted) Ph, heteroaryl, naphthyl, fluorenyl, diphenylmethyl, (substituted) phenylalkyl, heteroarylalkyl; R3 = H, alkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, (substituted) Ph, phenylalkyl, naphthyl, naphthylalkyl, heteroaryl, heteroarylalkyl; R4, R5, R7 = H, alkyl; R6 = H, alkyl, alkenyl], were prepared. Thus, title compound (II) [preparation starting from (S)-alanine Me ester hydrochloride given] inhibited RANTES binding in a CCR5 membrane binding assay with  $K_i = 9.97$  nM.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:367287 HCAPLUS

DOCUMENT NUMBER: 136:369611



TITLE: Preparation of piperidine derivatives as CCR5 antagonists

INVENTOR(S): Baroudy, Bahige M.; Clader, John W.; Josien, Hubert B.; McCombie, Stuart W.; McKittrick, Brian A.; Miller, Michael W.; Neustadt, Bernard R.; Palani, Anandan; Steensma, Ruo; Tagat, Jayaram R.; Vice, Susan F.; Laughlin, Mark A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S., 91 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

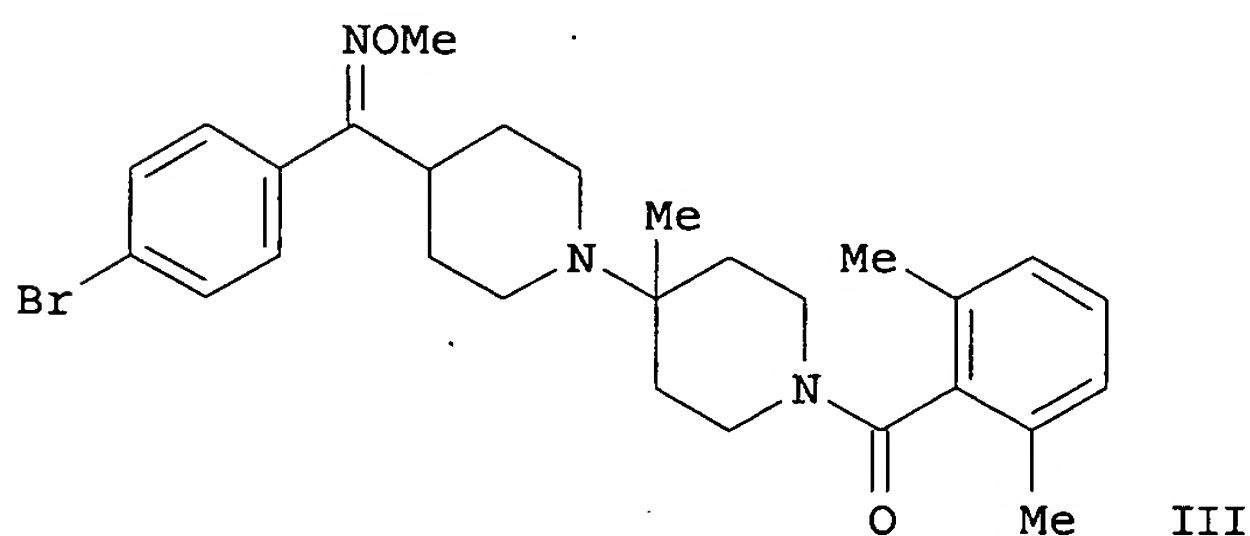
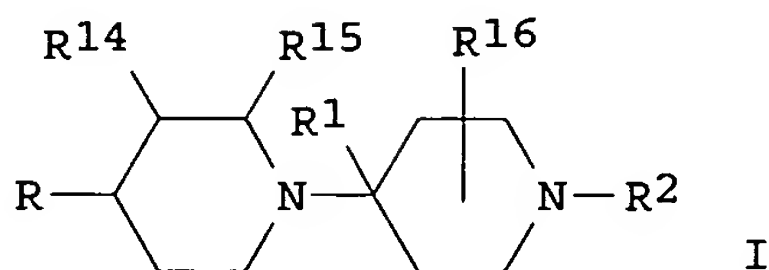
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6387930	B1	20020514	US 2000-562815	20000501
US 2003004185	A1	20030102	US 2001-10481	20011108
US 6602885	B2	20030805		

PRIORITY APPLN. INFO.: US 1999-132510P P 19990504  
US 2000-562815 A3 20000501

OTHER SOURCE(S): MARPAT 136:369611  
GI



AB Title compds. [I; R = XaRa; Ra = (un)substituted Ph, -pyridyl, -thienyl, -naphthyl; R1 = H or alk(en)yl; R3 = COR2; R2 = halo, alkyl, (un)substituted Ph, ZR7, etc.; R7 = halo, OH, alkyl, OMe, etc.; R14-R16 = H or alkyl; Xa = (un)substituted alkylene, O, CO, NH, etc.; Z = (un)substituted heteroarylene] were prepared. Thus, PhBr was acylated by N-trifluoroacetylpiperidine-4-carbonyl chloride and the O-protected-N-deprotected product condensed with N-Boc-4-piperidone in the presence of Ti(OPr)<sub>4</sub> followed by treatment with Et<sub>2</sub>AlCN to give, after MeMgBr treatment, I [R = 4-BrC<sub>6</sub>H<sub>4</sub>C(R<sub>4</sub>)<sub>2</sub>, R1 = Me, R14-R16 = H] (II; R3 = CO<sub>2</sub>Me<sub>3</sub>, R<sub>4</sub>R<sub>4</sub> = OCH<sub>2</sub>CH<sub>2</sub>O). The latter was O- and N-deprotected and the product converted in 3 steps to II (R3 = H, R<sub>4</sub>R<sub>4</sub> = NOME) which was

amidated by 2,6-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CO<sub>2</sub>H to give title compds. (E)- and (Z)-III. Data for biol. activity of I were given.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:59018 HCAPLUS

DOCUMENT NUMBER: 136:262969

TITLE: Synthesis of Mono- and Difluoronaphthoic Acids

AUTHOR(S): Tagat, Jayaram R.; McCombie, Stuart W.; Nazareno, Dennis V.; Boyle, Craig D.; Kozlowski, Joseph A.; Chackalamannil, Samuel; **Josien, Hubert**; Wang, Yuguang; Zhou, Guowei

CORPORATE SOURCE: Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA

SOURCE: Journal of Organic Chemistry (2002), 67(4), 1171-1177  
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:262969

AB Aryl carboxamides are useful structural units found in several biol. active compds. Unlike their benzoic acid counterparts, fluorinated versions of naphthoic acids are relatively unknown. In connection with a recent project, we needed viable syntheses of several mono- and difluorinated naphthoic acids. Herein we describe the synthesis of 5-, 6-, 7-, and 8-fluoro-1-naphthalenecarboxylic acids and 5,7-, 5,8-, 6,7-, and 4,5-difluoro-1-naphthalenecarboxylic acids. The 5-fluoronaphthoic acid was obtained from the corresponding 5-bromo compound via electrophilic fluorination of the lithio-intermediate. The remaining 6-fluoro-, 7-fluoro-, 8-fluoro-, 5,7-difluoro-, 5,8-difluoro- and 6,7-difluoronaphthoic acids were prepared by a new, general route involving conversion of com. fluorinated phenylacetic acids to 2-(fluoroaryl)glutaric acids with differential ester groups; selective hydrolysis to a mono acid, intramol. Friedel-Crafts cyclization, and aromatization furnished the target structures. An alternative process to assemble a naphthalene skeleton is also presented for the 5,7-difluoro- and 5,8-difluoronaphthoic acids. Finally, 4,5-difluoro-1-naphthalenecarboxylic acid was prepared expeditiously from 1,8-diaminonaphthalene by adapting classical reactions.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:639925 HCAPLUS

TITLE: Synthesis, SAR, and biological evaluation of 4-phenylpiperidine oximes as CCR5 antagonists for the treatment of HIV-1 infection

AUTHOR(S): Palani, Anandan; Shapiro, Sherry; Clader, John W.; Greenlee, William J.; **Josien, Hubert**; Bara, Tom; Cox, Kathleen; Baroudy, Bahige

CORPORATE SOURCE: Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-106. American Chemical Society: Washington, D. C.

CODEN: 69BUZP

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB The interaction of HIV-1 with the chemokine receptor CCR5 is required for the entry of the virus into macrophages. It is hoped that CCR5 antagonists which block viral entry will represent a new class of anti-HIV-1 agents with potential use in the prevention and treatment of HIV infection. This presentation will outline the synthesis and structure-activity relationship of 4-substituted Ph piperidine oximes, which are potent and selective CCR5 antagonists.

L34 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:639830 HCAPLUS

TITLE: Pharmacokinetic improvement of benzylidene ketal M2 muscarinic receptor antagonists via aryl amide modification

AUTHOR(S): Boyle, Craig D.; Vice, Susan F.; Chackalamannil, Samuel; Clader, John W.; Ford, Jennifer; Greenlee, William J.; Josien, Hubert B.; McCombie, Stuart W.; Nazareno, Dennis V.; Tagat, Jayram R.; Wang, Yuguang; Billard, William; Binch, Herbert, III; Crosby, Gordon; Cohen-Williams, Mary; Coffin, Vicki L.; Cox, Kathleen A.; Grotz, Diane E.; Duffy, Ruth A.; Ruperto, Vilma; Lachowicz, Jean E.

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), MEDI-011. American Chemical Society: Washington, D. C.

CODEN: 69BUZP

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB The senile dementia associated with Alzheimer's disease (AD) is correlated with diminished levels of synaptic acetylcholine (ACh) in the brain. Currently available pharmacotherapy for AD addresses this issue using inhibitors of acetylcholinesterase, which is the enzyme responsible for the degradation of ACh. Elevation of synaptic ACh levels could also be achieved by selectively inhibiting presynaptic muscarinic receptors of the M2 subtype, agonist-induced stimulation of which shuts off ACh release. Such an agent must be selective for the M2 receptor, as inhibition of M1 and M3 receptors causes undesired side effects. Previously, we have reported the initial discovery of a novel class of stabilized benzylidene ketal M2 receptor antagonists. We will discuss new targets consisting of aryl amide modifications which not only improved M2 binding and selectivity, but also enhanced the pharmacokinetic properties of the series. These changes led to the discovery of a highly potent and selective M2 antagonist, which demonstrated in vivo efficacy and had good bioavailability in multiple species.

L34 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:628993 HCAPLUS

DOCUMENT NUMBER: 136:47959

TITLE: Metabolic stabilization of benzylidene ketal M2 muscarinic receptor antagonists via halonaphthoic acid substitution

AUTHOR(S): Boyle, C. D.; Chackalamannil, S.; Clader, J. W.; Greenlee, W. J.; Josien, H. B.; Kaminski, J. J.; Kozlowski, J. A.; McCombie, S. W.; Nazareno, D. V.; Tagat, J. R.; Wang, Y.; Zhou, G.; Billard, W.; Binch, H.; Crosby, G.; Cohen-Williams, M.; Coffin, V. L.; Cox, K. A.; Grotz, D. E.; Duffy, R. A.; Ruperto, V.; Lachowicz, J. E.

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ,  
07033, USA  
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001),  
11(17), 2311-2314  
CODEN: BMCLE8; ISSN: 0960-894X  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The potential toxicol. liabilities of a previously studied M2 muscarinic antagonist benzylidene ketal were addressed by replacing the methylenedioxyphenyl moiety with a p-methoxyphenyl group, resulting in M2 selective compds. such as (I). Several halogenated naphthamide derivs. of I were studied to improve the pharmacokinetic profile via blockage of oxidative metabolism. Compound (II) demonstrated excellent M2 affinity and selectivity, human microsomal stability, and oral bioavailability in rodents and primates.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:201922 HCAPLUS  
TITLE: Discovery of potent, orally bioavailable CCR5 antagonists - 2  
AUTHOR(S): Palani, A.; Shapiro, S.; Josien, H.; Bara, T.; Clader, J.; Greenlee, W.; Tagat, J.; Steensma, R.; McCombie, S.; Neustadt, B.; Pushpavanam, P.; Chan, T. M.; Evans, A.; Blythin, D.; Ganguly, A.; Piwinski, J.; Dan, N.; Baroudy, B.; Endres, M.; Strizki, J.; Vantuno, N.; Cox, Kathleen; Broske, L.; Zhang, X.  
CORPORATE SOURCE: Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA  
SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001)  
MEDI-027  
CODEN: 69FZD4  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal; Meeting Abstract  
LANGUAGE: English

AB Inhibition of the interaction of HIV-1 with the chemokine receptor CCR5 is required for the entry of the virus into macrophages. It is hoped that CCR5 antagonists which block viral entry will represent a new class of anti-HIV-1 agents with potential use in the prevention and treatment of HIV infection. This presentation will outline the synthesis and structure-activity relationships of a series of piperidine amides, which are potent and selective CCR5 antagonists. Among these is SCH-C, a selective CCR5 antagonist with potent activity in RANTES binding ( $K_i=2$  nM), viral entry ( $IC_{50}=0.69$  nM) and replication assays ( $IC_{50}=0.06$  to  $6.5$  nM). SCH-C, which shows excellent oral bioavailability (>50%) in rats, dogs and monkeys, is a potential agent for the treatment of HIV infection.

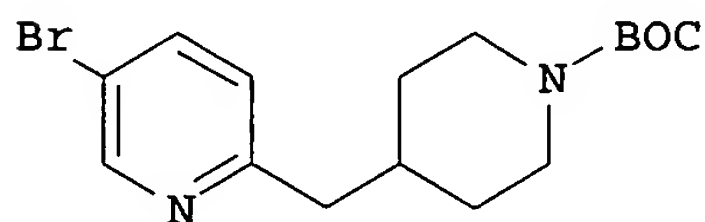
L34 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:201921 HCAPLUS  
TITLE: Discovery of potent, orally bioavailable CCR5

antagonists - 1  
 AUTHOR(S): Tagat, J.; Nazareno, D.; Vice, S.; Lin, S.; Steensma, R.; Miller, M.; Bauer, A.; McCombie, S.; Palani, A.; Josien, H.; Clader, J.; Neustadt, B.; Greenlee, W.; Ganguly, A.; Piwinski, J.; Chan, T. M.; Evans, A.; Dan, N.; Baroudy, B.; Endres, M.; Strizki, J.; Vantuno, N.; Cox, K.; Broske, L.; Zhang, X.  
 CORPORATE SOURCE: Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA  
 SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001)  
 MEDI-026  
 CODEN: 69FZD4  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal; Meeting Abstract  
 LANGUAGE: English

AB The interaction of HIV-1 with the transmembrane chemokine receptor CCR5 is known to be a crucial event in the process whereby the virus gains entry to macrophages. It is therefore expected that blockade of this interaction will prevent viral entry, and that mols. which affect this blockade will provide a new class of anti-HIV-1 agents with a mechanism of action distinct from currently used, intracellular protease and reverse-transcriptase inhibitors. Beginning with leads discovered in high-throughput screening, a series of piperidine amides was identified that are potent antagonists of the human CCR5 receptor. The synthesis, structure-activity relationships and antiviral activity of this antagonist series will be described.

L34 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2001:156283 HCAPLUS  
 DOCUMENT NUMBER: 134:326383  
 TITLE: Concise formation of 4-benzyl piperidines and related derivatives using a Suzuki protocol  
 AUTHOR(S): Vice, Susan; Bara, Tom; Bauer, Annette; Evans, C. Anderson; Ford, Jennifer; Josien, Hubert; McCombie, Stuart; Miller, Michael; Nazareno, Dennis; Palani, Anandan; Tagat, Jay  
 CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA  
 SOURCE: Journal of Organic Chemistry (2001), 66(7), 2487-2492  
 CODEN: JOCEAH; ISSN: 0022-3263  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 134:326383  
 GI



AB An efficient method of constructing 4-benzyl piperidines and related substances, e.g. I, is described. Thus, hydroboration of N-Boc-4-methylenepiperidine followed by reaction with PdCl<sub>2</sub>dppf/Ph<sub>3</sub>As/DMF/H<sub>2</sub>/K<sub>2</sub>CO<sub>3</sub> and 2,5-dibromopyridine gave I in 96% yield. This protocol tolerates a wide variation in both reaction partners and



complements the related process of Zhou and Keana.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:70475 HCAPLUS

DOCUMENT NUMBER: 134:266460

TITLE: The cascade radical annulation approach to new  
analogues of camptothecins: Combinatorial synthesis of  
silatecans and homosilatecans

AUTHOR(S): Curran, Dennis P.; Josien, Hubert; Bom,  
David; Gabarda, Ana E.; Du, Wu

CORPORATE SOURCE: Department of Chemistry and Center for Combinatorial  
Chemistry, University of Pittsburgh, Pittsburgh, PA,  
15260, USA

SOURCE: Annals of the New York Academy of Sciences (2000),  
922(Camptothecins), 112-121  
CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: New York Academy of Sciences

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 30 refs. on the cascade radical annulation approach to the  
camptothecin, combinatorial synthesis of silatecans and homosilatecans.  
This combinatorial synthetic approach involves two key steps: (1)  
N-propargylation of a lactone/pyridone D/E ring fragment and (2) cascade  
radical annulation of an A-ring isonitrile to form rings B and C. The  
synthesis is probably the most flexible and general route to the  
camptothecin class of mols. The parallel synthesis of several libraries  
of silatecan and homosilatecan libraries is summarized. One of the  
first-generation silatecans, DB-67, is emerging as a serious candidate for  
cancer chemotherapy.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:819476 HCAPLUS

DOCUMENT NUMBER: 133:362876

TITLE: Methods for preparation of camptothecin analogs having  
antitumor activity

INVENTOR(S): Curran, Dennis P.; Josien, Hubert; David,  
Bom

PATENT ASSIGNEE(S): University of Pittsburgh, USA

SOURCE: U.S., 24 pp., Cont.-in-part of U. S. Ser. No. 436,799.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6150343	A	20001121	US 1997-921102	19970829
US 6211371	B1	20010403	US 1998-7872	19980115
CA 2302226	AA	19990304	CA 1998-2302226	19980826
WO 9909996	A1	19990304	WO 1998-US17683	19980826
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,				
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,				
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,				
UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

Ward 10\_663042-inventor search

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9892056	A1	19990316	AU 1998-92056	19980826
AU 760543	B2	20030515		
EP 1017399	A1	20000712	EP 1998-944535	19980826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001513567	T2	20010904	JP 2000-507386	19980826
US 6136978	A	20001024	US 1998-212178	19981215
US 6455699	B1	20020924	US 2000-633561	20000807
US 2001029298	A1	20011011	US 2001-815459	20010323
US 6620937	B2	20030916		
US 2002193598	A1	20021219	US 2002-134781	20020429
US 6743917	B2	20040601		
US 2003105324	A1	20030605	US 2002-251153	20020920
US 2004029835	A1	20040212	US 2003-629432	20030729
US 2004063947	A1	20040401	US 2003-663605	20030916

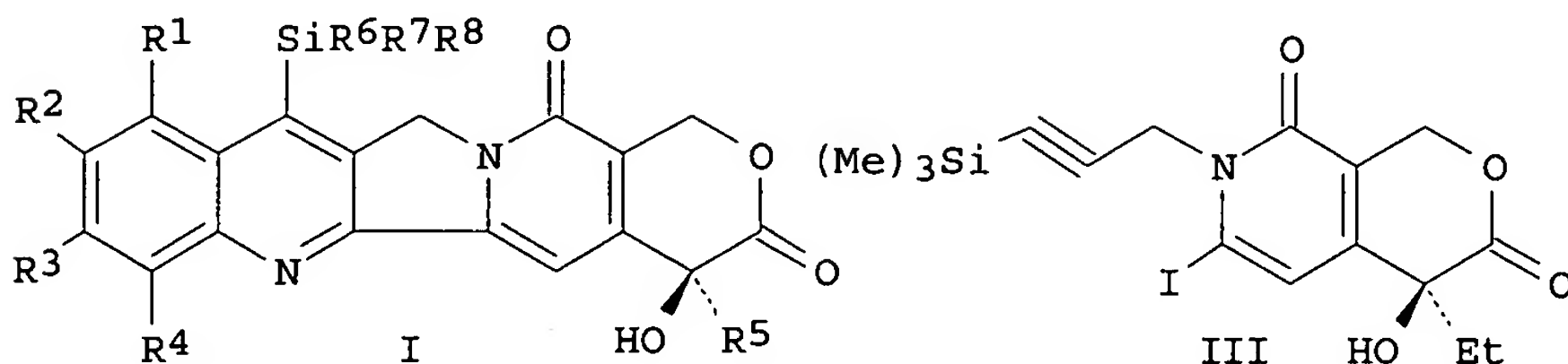
PRIORITY APPLN. INFO.:

US 1993-85190	A2	19930630
US 1995-436799	A2	19950508
US 1997-921102	A	19970829
US 1998-7872	A3	19980115
WO 1998-US17683	W	19980826
US 1998-212178	A1	19981215
US 2000-613968	B1	20000711
US 2000-633561	A1	20000807
US 2001-815459	A3	20010323
US 2002-251153	B1	20020920

OTHER SOURCE(S):

CASREACT 133:362876; MARPAT 133:362876

GI



AB Camptothecin derivs. [I; R1 = H, alkyl, alkenyl, alkynyl, alkoxy, aryloxy, carbamoyloxy, halogen, OH, NO2, CN, N3, CHO, hydrazino, -C(O)Rf {Rf = alkyl, haloalkyl, alkoxy, NH2, OH}, NH2, -SRc {Rc = H, -C(O)Rf, alkyl, aryl, -OC(O)Rd or -OC(O)ORD (Rd = alkyl) etc.,}; R2 = OH; R3 = H, F, halogen, NO2, NH2, OH, CN; R4 = H, F, alkyl, alkenyl, alkynyl, alkoxy; R5 = alkyl, propargyl; R6, R7, R8 = alkyl, alkenyl group, alkynyl, aryl or a -(CH2)nR9 group, wherein n is an integer within the range of 1 through 10 and R9 = OH, alkoxy, amino, alkylamino, dialkylamino, halogen, CN, NO2] and their pharmaceutically acceptable salts were prepared as antitumor agents. Thus, [I; R1-R4 = H, R5 = Et, R6-R8 = Me (II)] was prepared via reaction of (III) and Ph isonitrile. II was tested for antitumor activity [IC50 = 3.8 nm vs HL-60 cells; IC50 = 5.6 nm vs. 833K cells; IC50 = 4.2 nm vs DC-3F cells].

REFERENCE COUNT:

13

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:790477 HCAPLUS

DOCUMENT NUMBER: 133:350146

TITLE: Preparation of piperidine derivatives as CCR5 antagonists

INVENTOR(S): Baroudy, Bahige M.; Clader, John W.; Josien, Hubert B.; McCombie, Stuart W.; McKittrick, Brian A.; Miller, Michael W.; Neustadt, Bernard R.; Palani, Anandan; Steensma, Ruof; Tagat, Jayaram R.; Vice, Susan F.; Laughlin, Mark A.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

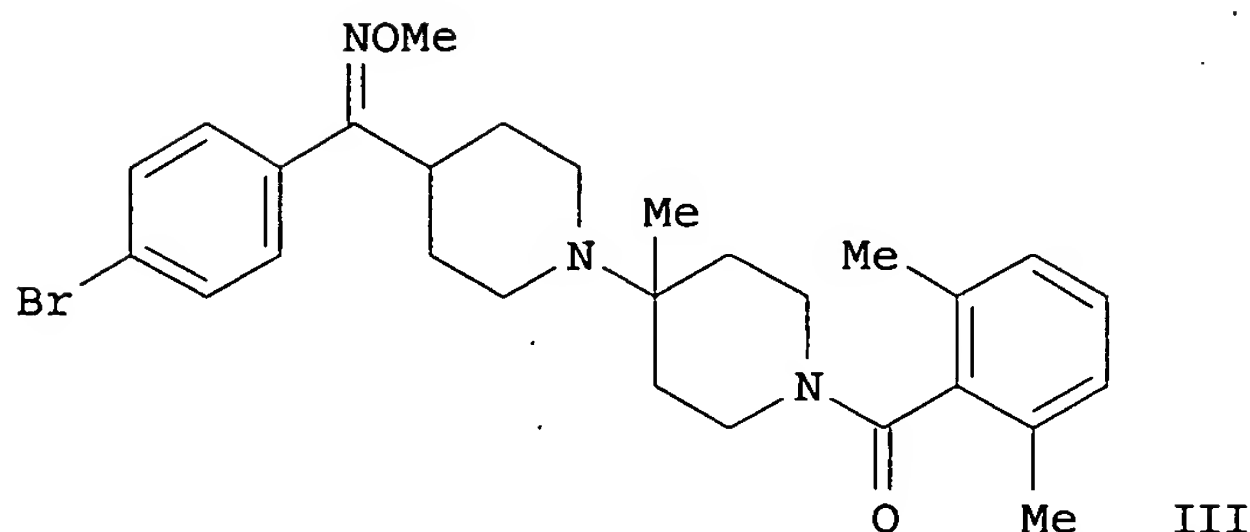
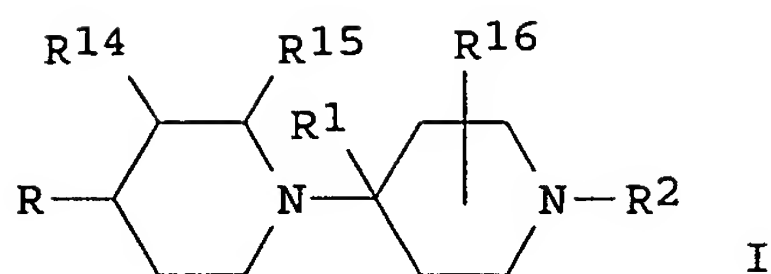
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066559	A1	20001109	WO 2000-US11633	20000501
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2371587	AA	20001109	CA 2000-2371587	20000501
EP 1175402	A1	20020130	EP 2000-926487	20000501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010607	A	20020213	BR 2000-10607	20000501
TR 200103213	T2	20020321	TR 2001-200103213	20000501
NZ 514675	A	20040528	NZ 2000-514675	20000501
TR 200402496	T2	20050124	TR 2004-200402496	20000501
ZA 2001008867	A	20030127	ZA 2001-8867	20011026
NO 2001005365	A	20020103	NO 2001-5365	20011102
PRIORITY APPLN. INFO.:			US 1999-305187	A2 19990504
			WO 2000-US11633	W 20000501
OTHER SOURCE(S):		MARPAT 133:350146		
GI				





AB Title compds. [I; R = XaRa; Ra = (un)substituted Ph, -pyridyl, -thienyl, -naphthyl; R1 = H or alk(en)yl; R3 = COR2; R2 = halo, alkyl, (un)substituted Ph, ZR7, etc.; R7 = halo, OH, alkyl, OMe, etc.; R14-R16 = H or alkyl; Xa = (un)substituted alkylene, O, CO, NH, etc.; Z = (un)substituted heteroarylene] were prepared. Thus, PhBr was acylated by N-trifluoroacetylpiperidine-4-carbonyl chloride and the O-protected-N-deprotected product condensed with N-Boc-4-piperidone in the presence of Ti(OPr)<sub>4</sub> followed by treatment with Et<sub>2</sub>AlCN to give, after MeMgBr treatment, I [R = 4-BrC<sub>6</sub>H<sub>4</sub>C(R<sub>4</sub>)<sub>2</sub>, R1 = Me, R14-R16 = H] (II; R3 = CO<sub>2</sub>Me<sub>3</sub>, R4R4 = OCH<sub>2</sub>CH<sub>2</sub>O). The latter was O- and N-deprotected and the product converted in 3 steps to II (R3 = H, R4R4 = NOMe) which was amidated by 2,6-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CO<sub>2</sub>H to give title compds. (E)- and (Z)-III. Data for biol. activity of I were given.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:790476 HCAPLUS

DOCUMENT NUMBER: 133:350248

TITLE: Preparation of piperazine derivatives useful as CCR5 antagonists

INVENTOR(S): Baroudy, Bahige M.; Clader, John W.; Josien, Hubert B.; McCombie, Stuart W.; Mckittrick, Brian A.; Miller, Michael W.; Neustadt, Bernard R.; Palani, Anandan; Smith, Elizabeth M.; Steensma, Ruofu; Tagat, Jayaram R.; Vice, Susan F.; Laughlin, Mark A.; Gilbert, Eric; Labroli, Marc A.

PATENT ASSIGNEE(S): Schering Corporation, USA; et al.

SOURCE: PCT Int. Appl., 109 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066558	A1	20001109	WO 2000-US11632	20000501

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,  
 CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN,  
 IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN,  
 MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
 TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2371583 AA 20001109 CA 2000-2371583 20000501  
 EP 1175401 A1 20020130 EP 2000-926486 20000501

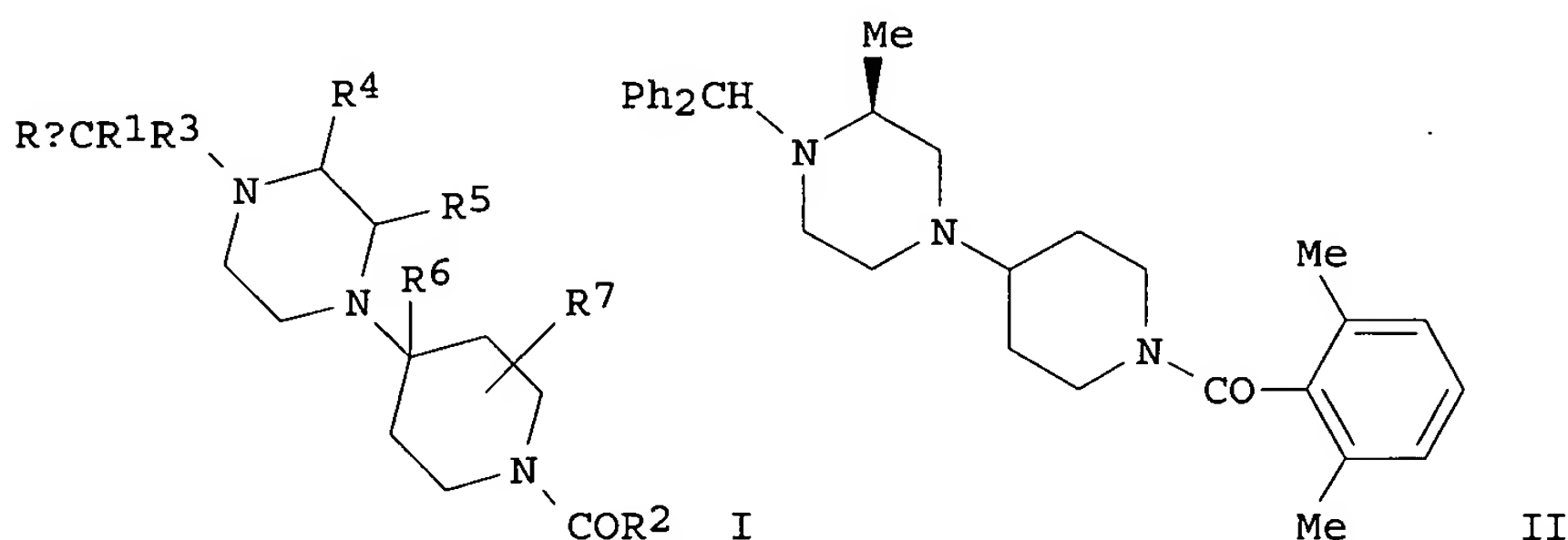
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO

BR 2000010304 A 20020213 BR 2000-10304 20000501  
 TR 200103214 T2 20020321 TR 2001-200103214 20000501  
 ZA 2001008868 A 20030127 ZA 2001-8868 20011026  
 NO 2001005366 A 20020103 NO 2001-5366 20011102

PRIORITY APPLN. INFO.:

US 1999-305226 A2 19990504  
 US 1999-305266 A 19990504  
 WO 2000-US11632 W 20000501

OTHER SOURCE(S): MARPAT 133:350248  
 GI



AB The title compds. I [Ra = optionally substituted Ph, pyridyl, thiophenyl, naphthyl; R1 = H, alkyl; R2 = substituted Ph, substituted heteroaryl, naphthyl, fluorenyl, diphenylmethyl or optionally substituted phenyl- or heteroarylalkyl; R3 = H, alkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, or optionally substituted Ph, phenylalkyl, naphthyl, naphthylalkyl, heteroaryl, heteroarylalkyl; R4, R5, R7 = H, alkyl; R6 = H, alkyl, alkenyl], CCR5 antagonists, were prepared E.g., piperazine derivative II was prepared

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:754523 HCAPLUS

DOCUMENT NUMBER: 133:322036

TITLE: Methods for preparation of camptothecin analogs having antitumor activity

INVENTOR(S): Curran, Dennis P.; Josien, Hubert; Bom, David; Burke, Thomas G.

PATENT ASSIGNEE(S): University of Pittsburgh, USA

SOURCE: U.S., 52 pp., Cont.-in-part of U.S. Ser. No. 921,102.  
 CODEN: USXXAM

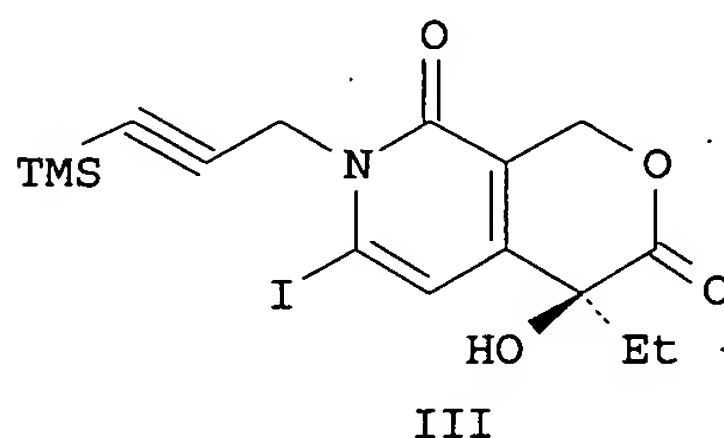
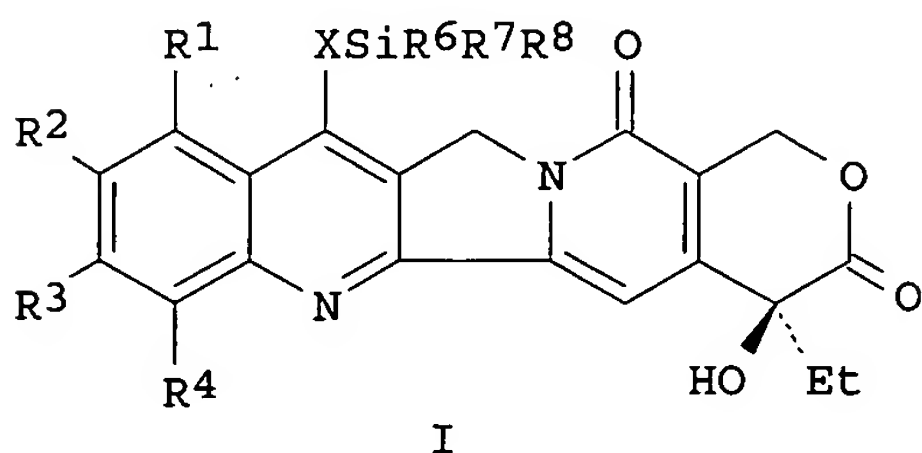
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6136978	A	20001024	US 1998-212178	19981215
US 6150343	A	20001121	US 1997-921102	19970829
CA 2353822	AA	20000622	CA 1999-2353822	19991215
WO 2000035924	A1	20000622	WO 1999-US29937	19991215
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140948	A1	20011010	EP 1999-965287	19991215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532505	T2	20021002	JP 2000-588183	19991215
AU 777786	B2	20041028	AU 2000-31236	19991215
NZ 512210	A	20041224	NZ 1999-512210	19991215
US 2001029298	A1	20011011	US 2001-815459	20010323
US 6620937	B2	20030916		
US 2002193598	A1	20021219	US 2002-134781	20020429
US 6743917	B2	20040601		
US 2004063947	A1	20040401	US 2003-663605	20030916
PRIORITY APPLN. INFO.:				
			US 1993-85190	B2 19930630
			US 1995-436799	B2 19950508
			US 1997-921102	A2 19970829
			US 1998-7872	A3 19980115
			US 1998-212178	A 19981215
			WO 1999-US29937	W 19991215
			US 2000-613968	B1 20000711
			US 2001-815459	A3 20010323

OTHER SOURCE(S): MARPAT 133:322036  
GI



AB Camptothecin derivs. [I; R<sub>1</sub>, R<sub>2</sub> = H, alkyl, alkenyl, benzyl, alkynyl, alkoxy, aryloxy, acyloxy, -OC(O)OR<sub>d</sub>, {R<sub>d</sub> = alkyl, carbamoyloxy, halogen, OH, NO<sub>2</sub>, CN, N<sub>3</sub>, CHO, NH<sub>2</sub>, -SR<sub>c</sub> (R<sub>c</sub> = H, acyl, alkyl, aryl etc.,)}; R<sub>3</sub> = H, halogen, NO<sub>2</sub>, NH<sub>2</sub>, OH, CN; or R<sub>1</sub> + R<sub>2</sub> or R<sub>2</sub> + R<sub>3</sub> together form a group of the formula -O(CH<sub>2</sub>)<sub>n</sub>O- wherein n represents the integer 1 or 2; R<sub>4</sub> = H, a trialkylsilyl group, F, alkyl, alkenyl, alkynyl, alkoxy; R<sub>5</sub> = alkyl, allyl, benzyl, propargyl; R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> = alkyl, alkenyl group, alkynyl, aryl

or a -(CH<sub>2</sub>)<sub>n</sub>R<sub>9</sub> group, wherein n is an integer within the range of 1 through 10 and R<sub>9</sub> = OH, alkoxy, amino, alkyl, dialkylamino, halogen, CN, NO<sub>2</sub>; X = R<sub>11</sub>, bond; R<sub>11</sub> = alkylene, alkenylene] and their pharmaceutically acceptable salts were prepared as antitumor agents. Thus, [I; R<sub>1</sub>-R<sub>4</sub> = H, XSiR<sub>6</sub>R<sub>7</sub>R<sub>8</sub> = TMS (II)] was prepared via reaction of III and Ph isonitrile. II was tested for antitumor activity [IC<sub>50</sub> = 3.8 nm vs HL-60 cells; IC<sub>50</sub> = 5.6 nm vs. 833K cells; IC<sub>50</sub> = 4.2 nm vs DC-3F cells].

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:421147 HCAPLUS

DOCUMENT NUMBER: 133:43697

TITLE: Preparation of camptothecin analogs for use as antitumor agents

INVENTOR(S): Curran, Dennis P.; Josien, Hubert; Bom, David; Burke, Thomas G.

PATENT ASSIGNEE(S): University of Pittsburgh, USA

SOURCE: PCT Int. Appl., 144 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

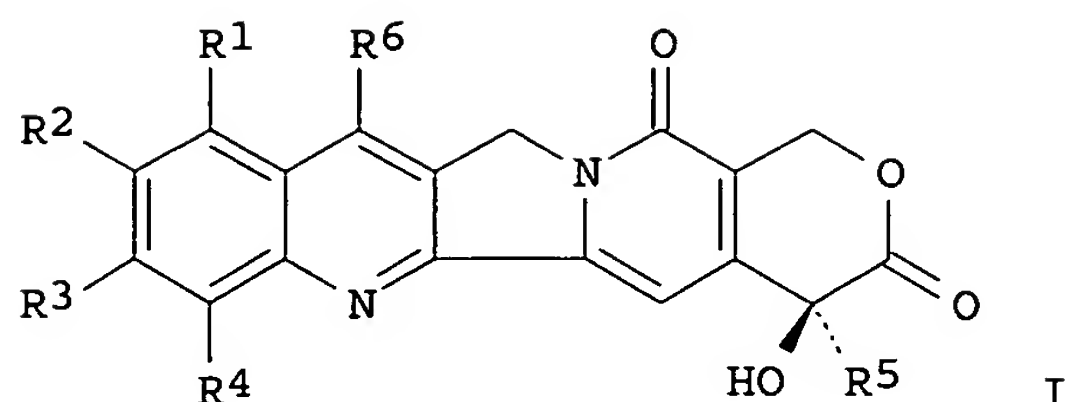
FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035924	A1	20000622	WO 1999-US29937	19991215
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6136978	A	20001024	US 1998-212178	19981215
CA 2353822	AA	20000622	CA 1999-2353822	19991215
EP 1140948	A1	20011010	EP 1999-965287	19991215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532505	T2	20021002	JP 2000-588183	19991215
AU 777786	B2	20041028	AU 2000-31236	19991215
NZ 512210	A	20041224	NZ 1999-512210	19991215
PRIORITY APPLN. INFO.:			US 1998-212178	A 19981215
			US 1993-85190	B2 19930630
			US 1995-436799	B2 19950508
			US 1997-921102	A2 19970829
			WO 1999-US29937	W 19991215

OTHER SOURCE(S): MARPAT 133:43697

GI



AB Camptothecin analogs I [R1, R2 = H, OH, NO<sub>2</sub>, CN, N<sub>3</sub>, CHO, NH<sub>2</sub>, NHNH<sub>2</sub>, SH, alkyl, alkenyl, alkynyl, alkoxy, aryloxy, acyloxy, acyl, carbamoyloxy, halogen, acylthio, alkylthio, arylthio, etc.; R3 = H, NO<sub>2</sub>, NH<sub>2</sub>, OH, CN, halogen; R2R3 = O(CH<sub>2</sub>)<sub>n</sub>O, n = 1, 2; R4 = H, F, alkyl, alkenyl, alkynyl, trialkylsilyl, alkoxy; R5 = allyl, benzyl, propargyl, alkyl; R6 = trialkylsilyl, trialkylsilylalkyl, etc.] were prepared for use as anticancer agents. Thus, I (R1-4 = H, R5 = Et, R6 = SiMe<sub>3</sub>) was prepared starting from (4S)-4-ethyl-4-hydroxy-6-iodo-1H-pyrano[3,4-c]pyridine-3,8(4H,7H)-dione and (3-bromo-1-propynyl)trimethylsilane. The prepared camptothecin analogs were tested for inhibition of growth of HL-60, 883K, and DC-3F cancer cell lines, for enhancement of topoisomerase I mediated DNA cleavage, and for inhibition of topoisomerase I mediated DNA relaxation.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:172606 HCAPLUS

DOCUMENT NUMBER: 130:209844

TITLE: Preparation of camptothecin analogs for use as antitumor agents

INVENTOR(S): Curran, Dennis P.; Josien, Hubert; Bom, David

PATENT ASSIGNEE(S): University of Pittsburgh, USA

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909996	A1	19990304	WO 1998-US17683	19980826
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6150343	A	20001121	US 1997-921102	19970829
CA 2302226	AA	19990304	CA 1998-2302226	19980826
AU 9892056	A1	19990316	AU 1998-92056	19980826
AU 760543	B2	20030515		
EP 1017399	A1	20000712	EP 1998-944535	19980826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001513567	T2	20010904	JP 2000-507386	19980826

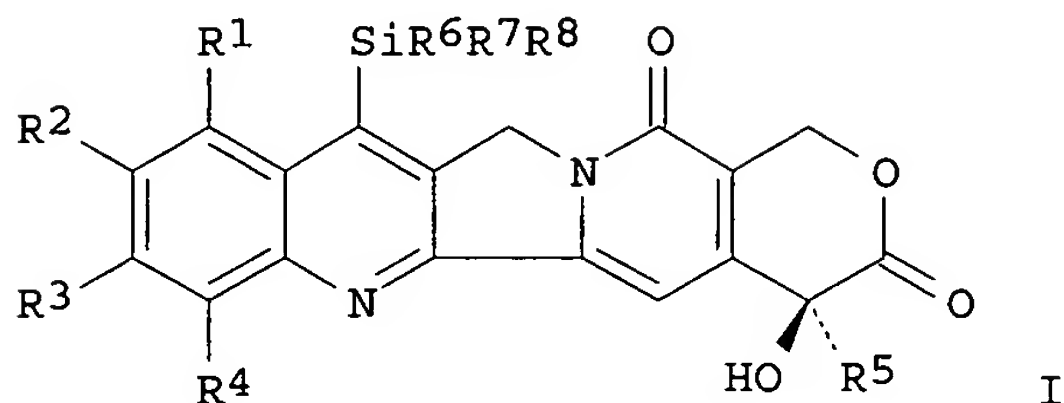
## PRIORITY APPLN. INFO.:

US 1997-921102	A 19970829
US 1993-85190	A2 19930630
US 1995-436799	A2 19950508
WO 1998-US17683	W 19980826

## OTHER SOURCE(S):

MARPAT 130:209844

GI



AB Camptothecin analogs I [R1, R2 = H, OH, NO2, CN, N3, NH2, CHO, NHNH2, SH, benzyl, alkyl, alkenyl, alkynyl, alkoxy, aryloxy, acyloxy, carbamoyloxy, halogen, acyl, alkylthio, acylthio, arylthio; R1R2 = -O(CH2)nO-; n = 1, 2; R3 = H, NO2, NH2, OH, CN; R2R3 = -O(CH2)nO-; n = 1, 2; R4 = H, F, alkyl, alkenyl, alkynyl, alkoxy; R5 = propargyl, alkyl; R6, R7, R8 = alkyl, alkenyl, alkynyl, aryl, -(CH2)mR9; m = 1-10; R9 = OH, NH2, CN, NO2, alkoxy, alkylamino, dialkylamino, halogen] were prepared for use as antitumor agents. Thus, (20S)-7-(trimethylsilyl)camptothecin was prepared in 85% yield by cyclization of (4S)-4-ethyl-4-hydroxy-6-iodo-1H-pyrano[3,4-c]pyridine-3,8(4H,7H)-dione with Me3SiC.tplbond.CCH2Br in DME and DMF at 0°. The prepared compds. were tested for enhancement and inhibition of topoisomerase I activity and for inhibition of cancer cell growth of HL-60, 833K, and DC-3F cell lines.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:646607 HCAPLUS

DOCUMENT NUMBER: 130:66743

TITLE: Design of constrained analogs of amino acids and their incorporation in the sequence of substance P

AUTHOR(S): Ayoub, Mimoun; Brunissen, Alie; Josien, Hubert

; Loffet, Albert; Chassaing, Gerard; Lavielle, Solange  
CORPORATE SOURCE: Laboratoire de Chimie Organique Biologique, CNRS URA 493, Universite P. et M. Curie, Paris, 75005, Fr.

SOURCE: Actualites de Chimie Therapeutique (1996), 22, 83-92  
CODEN: ACHTD9; ISSN: 0338-8999

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 15 refs. describing strategies developed by the authors for the preparation of non-proteinogenic amino acids, i.e. rotomeric probes of phenylalanine and  $\alpha$ -methylated amino acids, are described. These amino acids have been incorporated into a substance P analog in order to probe the space fillings of the S7 and S8 binding subsites of the neurokinin-1 receptor and the importance of a reinforcement of  $\alpha$ -helical structures on activity.

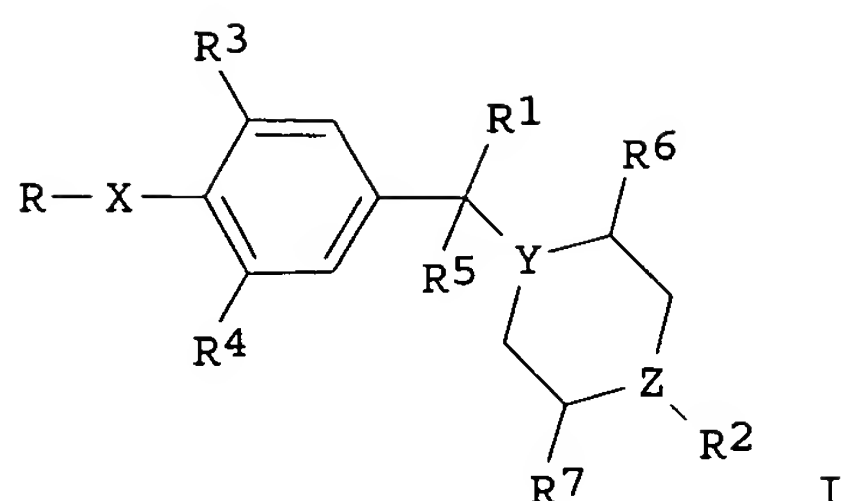
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN



ACCESSION NUMBER: 1998:112193 HCAPLUS  
 DOCUMENT NUMBER: 128:180426  
 TITLE: Preparation of piperazine and piperidine derivatives  
 as muscarinic antagonists  
 INVENTOR(S): Lowe, Derek B.; Chang, Wei K.; Kozlowski, Joseph A.;  
 Berger, Joel G.; McQuade, Robert; Barnett, Allen;  
 Sherlock, Margaret; Tom, Wing; Dugar, Sundeep; Chen,  
 Lian-yong; Clader, John W.; Chackalamannil, Samuel;  
 Wang, Yuguang; McCombie, Stuart W.; Tagat, Jayaram R.;  
 Vice, Susan F.; Vaccaro, Wayne D.; Green, Michael J.;  
 Browne, Margaret E.; Asberom, Theodros; Boyle, Craig  
 D.; **Josien, Hubert B.**  
 PATENT ASSIGNEE(S): Schering Corp., USA  
 SOURCE: PCT Int. Appl., 156 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805292	A2	19980212	WO 1997-US13383	19970806
WO 9805292	A3	19980402		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5889006	A	19990330	US 1996-700628	19960808
CA 2261725	AA	19980212	CA 1997-2261725	19970806
AU 9738999	A1	19980225	AU 1997-38999	19970806
AU 724001	B2	20000907		
EP 938483	A2	19990901	EP 1997-936296	19970806
EP 938483	B1	20030226		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO				
BR 9711119	A	19991123	BR 1997-11119	19970806
JP 2000501117	T2	20000202	JP 1998-508038	19970806
NZ 333801	A	20000428	NZ 1997-333801	19970806
AT 233260	E	20030315	AT 1997-936296	19970806
NO 9900551	A	19990407	NO 1999-551	19990205
HK 1018776	A1	20030829	HK 1999-103789	19990902
PRIORITY APPLN. INFO.:				
			US 1996-700628	A 19960808
			US 1995-392697	B2 19950223
			US 1995-457712	B2 19950602
			US 1996-602403	A2 19960216
			WO 1997-US13383	W 19970806
OTHER SOURCE(S): MARPAT 128:180426				
GI				



AB Title compds. I (R = OH, HOCH<sub>2</sub>, etc.; R<sub>1</sub> = H, alkyl, alkenyl, cyano, etc.; R<sub>2</sub> = H, (un)substituted piperidine; R<sub>3</sub> = cycloalkylalkyl, haloacyl, benzyloxalkyl, etc.; R<sub>4</sub> = H, halo, alkyl, alkoxy, etc.; R<sub>5</sub> = H, alkyl, alkenyl, cyano, etc.; R<sub>1</sub>-R<sub>5</sub> = (un)substituted saturated (hetero)cyclic ring; R<sub>6</sub> = H, alkyl, hydroxyalkyl, arylalkyl, aminoalkyl, etc.; R<sub>7</sub> = indolylalkyl, carboxyalkyl, etc.; X = O, S, SO, SO<sub>2</sub>, CO, CS, NHCOO, etc.; RX = I, Br, alkylcarbonyl, etc.; Y = N, CH, C-alkyl; Z = N, CH, C-alkyl), including isomers, salts, esters, and solvates, are prepared and are defined muscarinic antagonists useful for treating cognitive disorders such as Alzheimer's disease. Pharmaceutical compns. and methods of preparation are also disclosed. Also disclosed are synergistic combinations of I with acetylcholinesterase inhibitors.

L34 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:63390 HCAPLUS

DOCUMENT NUMBER: 128:154267

TITLE: A general synthetic approach to the (20S)-camptothecin family of antitumor agents by a regiocontrolled cascade radical cyclization of aryl isonitriles

AUTHOR(S): Josien, Hubert; Ko, Sung-Bo; Bom, David; Curran, Dennis P.

CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA

SOURCE: Chemistry--A European Journal (1998), 4(1), 67-83  
CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:154267

AB A general and efficient synthesis of (20S)-camptothecin (I) was reported. A key common intermediate containing the pyridone and lactone (DE) rings of camptothecin and most derivs. was constructed from 2-trimethylsilyl-6-methoxypyridine by a series of metalation reactions and a Heck cyclization to provide an achiral bicyclic enol ether. Sharpless asym. dihydroxylation followed by lactol oxidation and iododesilylation produced the key intermediate in 94% enantiomeric excess. Alkylation with propargyl bromide and a cascade radical reaction with PhNC then produced I. About 20 other penta- and hexacyclic analogs of camptothecin with differing single or multiple substituents at C7, C9, C10, C11, and/or C12 were made by changing the propargylating agent and the isonitrile. Included among these are several drug candidates and the approved drugs topotecan and irinotecan. The synthesis of the prodrug irinotecan is a direct one that does not pass through the active metabolite. The use of ortho-trimethylsilyl-substituted isonitriles allows the regioselective synthesis of camptothecin analogs in cases where isomeric mixts. are formed from the parent isonitriles. The synthesis of the derivs. relies



on the broad scope and functional group tolerance of the key cascade radical reaction.

REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:30511 HCAPLUS

DOCUMENT NUMBER: 128:175876

TITLE: 7-Silylcamptothecins (silatecans): a new family of camptothecin antitumor agents

AUTHOR(S): Josien, Hubert; Bom, David; Curran, Dennis P.; Zheng, Yu-Huang; Chou, Ting-Chao

CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(24), 3189-3194

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis and biol. evaluation of about one dozen 7-silylcamptothecin derivs. are described. Most new compds. show potencies comparable to or better than camptothecin itself. The best compound, 11-fluoro-10-amino-7-trimethylsilylcamptothecin, is more than 20 times more potent than camptothecin in cell assays.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:439256 HCAPLUS

DOCUMENT NUMBER: 127:95436

TITLE: Synthesis of (S)-mappicine and mappicine ketone via radical cascade reaction of isonitriles

AUTHOR(S): Josien, Hubert; Curran, Dennis P.

CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA

SOURCE: Tetrahedron (1997), 53(26), 8881-8886

CODEN: TETRAB; ISSN: 0040-4020

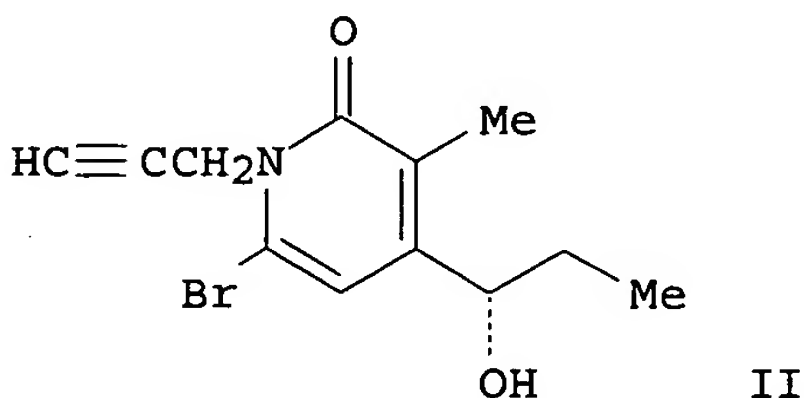
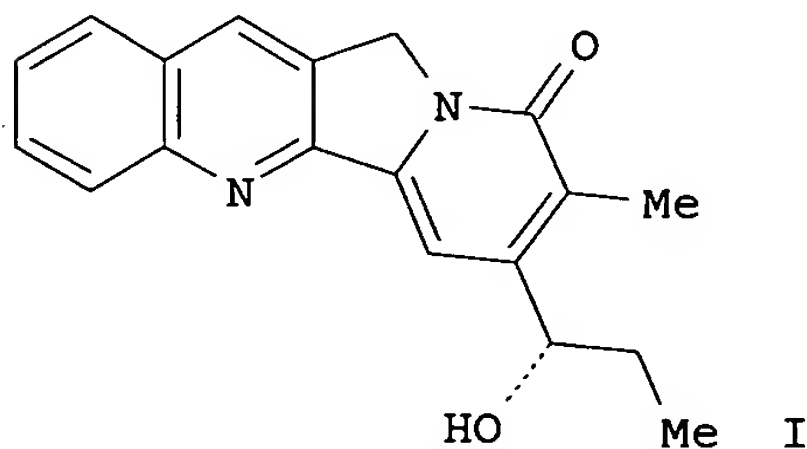
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 127:95436

GI



AB (S)-mappicine (I) and mappicine ketone were prepared from Me acetoacetate by a strategy featuring a radical cascade reaction of II with Ph isonitrile

as the key step. The introduction of the hydroxy group of (S)-mappicine occurred with moderate selectivity through asym. hydroxylation.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:108748 HCAPLUS

DOCUMENT NUMBER: 126:207591

TITLE: Tachykinin NK-1 receptor probed with constrained analogs of substance P

AUTHOR(S): Sagan, Sandrine; Josien, Hubert; Karoyan, Philippe; Brunissen, Alie; Chassaing, Gerard; Lavielle, Solange

CORPORATE SOURCE: Laboratoire de Chimie Organique Biologique, CNRS URA 493, Universite P. et M. Curie, Paris, 75005, Fr.

SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(12), 2167-2178

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The action of rotameric probes introduced either in position 7 or 8 in the sequence of substance P (SP) was investigated. i.e., L-tetrahydroisoquinoleic acid (Tic), L-fluorenylglycine (Flg), L-diphenylalanine (Dip), the diastereoisomers of L-1-indanylglycine (Ing) and L-benz[f]indanylglycine (Bfi), the Z- and E-isomers of dehydrophenylalanine and dehydronaphthylalanine ( $\Delta$ ZPhe,  $\Delta$ EPhe,  $\Delta$ ZNal,  $\Delta$ ENal) and L-o,o'-dimethylphenylalanine (Dmp). The aim this study was the topog. characterization of the binding subsites of human NK-1 receptor expressed in CHO cells, especially the S7 and S8 subsites, corresponding to residues Phe7 and Phe8 of substance P. According to the binding potencies of these substituted-SP analogs, the S7 binding subsite is smaller than the S8 subsite: the S7 subsite accepts only one aromatic nucleus, while the S8 can accommodate three coplanar nuclei altogether. These findings are compatible with the idea that the S8 binding subsite may reside in the extracellular loops of the hNK-1 receptor. NK-1 agonists bind to human NK-1 receptor and activate the production of both inositol phosphates and cAMP. As already quoted for septide, [pGlu6, Pro9]SP(6-11), discrepancies are observed between affinity ( $K_i$ ) and activity ( $EC_{50}$ ) values for IPs production. While a weak correlation between  $K_i$  and  $EC_{50}$  values for IPs production could be found ( $r = 0.70$ ), an excellent correlation could be demonstrated between their affinities ( $K_i$ ) and their potencies ( $EC_{50}$ ) for cAMP production ( $r = 0.97$ ). The high potency ( $EC_{50}$ ) observed for "septide-like" mols. on PI hydrolysis, compared to their affinity is not an artifact related to the high level of NK-1 receptors expressed on CHO cells since a good correlation was found between  $EC_{50}$  values obtained for PI hydrolysis and those measured for spasmogenic activity in guinea pig ileum bioassay ( $r = 0.94$ ).

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

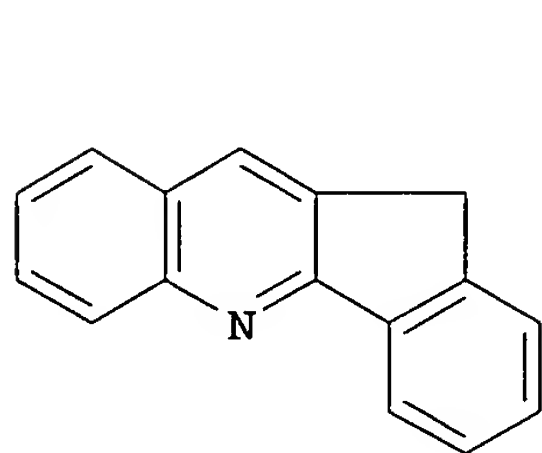
ACCESSION NUMBER: 1996:535176 HCAPLUS

DOCUMENT NUMBER: 125:276262

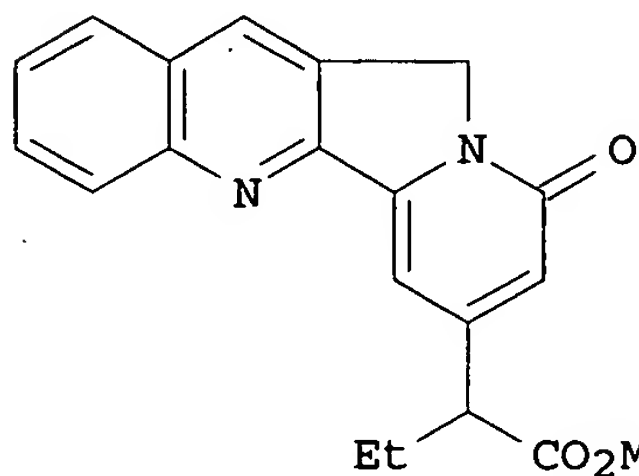
TITLE: Tandem radical reactions of isonitriles with 2-pyridonyl and other aryl radicals: scope and limitations, and a first generation synthesis of (+)-camptothecin

AUTHOR(S): Curran, Dennis P.; Liu, Hui; Josien, Hubert; Ko, Sung-Bo

CORPORATE SOURCE: Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260, USA  
 SOURCE: Tetrahedron (1996), 52(35), 11385-11404  
 CODEN: TETRAB; ISSN: 0040-4020  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 125:276262  
 GI



I

Et CO<sub>2</sub>Me II

AB Photolysis of N-propargyl-6-halo-2-pyridones and related aromatic halides in the presence of aryl isonitriles provides tetra- and penta-cyclic products, e.g. I and II, in a single step by a sequence of radical addition to the isonitrile followed by two cyclizations. The scope and limitations of the process are described along with a first generation synthesis of racemic camptothecin.

L34 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:463810 HCAPLUS  
 DOCUMENT NUMBER: 125:133045  
 TITLE: Topographic analysis of the S7 binding subsite of the tachykinin neurokinin-1 receptor  
 AUTHOR(S): Josien, Hubert; Convert, Odile; Berlose, Jean-Philippe; Sagan, Sandrine; Brunissen, Alie; Lavielle, Solange; Chassaing, Gerard  
 CORPORATE SOURCE: Lab. Chim., Univ. Pierre et Marie Curie, Paris, 75005, Fr.  
 SOURCE: Biopolymers (1996), 39(2), 133-147  
 CODEN: BIPMAA; ISSN: 0006-3525  
 PUBLISHER: Wiley  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Conformationally and configurationally restricted rotameric probes of phenylalanine have been incorporated in the sequence of substance P (SP)-Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH<sub>2</sub>-for analyzing the binding pockets of Phe7 (S7) and Phe8 (S8), in the neurokinin-1 receptor. These analogs of phenylalanine are (2S, 3R)- and (2S, 3S)-indanylglycines, E- and Z- $\alpha$ ,  $\beta$ -dehydrophenylalanines, and 2(S)- $\alpha$ ,  $\beta$ -cyclopropylphenylalanines [ $\Delta$ EPhe,  $\Delta$ ZPhe,  $\Delta$ E2(S)Phe, and  $\Delta$ Z2(S)Phe]. Binding data obtained with either conformationally (Ing diastereoisomers) or configurationally ( $\Delta$ EPhe,  $\Delta$ ZPhe) probes have unveiled large differences in the binding potencies of these rotameric probes. With the support of NMR data and energy calcns. done on these SP-substituted analogs, we attempt to answer questions inherent to such study. First, none of these six probes

prevents the formation of bioactive conformation (s) of the backbone of SP. Second, both diastereoisomers (S, S) and (S, R) of indanylglycine preferentially adopt, in the sequence of SP, the gauche(-) and trans side-chain orientations, resp., as previously postulated from energy calcns. with model peptides. However, in solution, the difference in energy between these rotamers included in the sequence of SP, compared to model peptides, is smaller since the other rotamer can be detected in [(2S, 3R)Ing7]SP. Finally, from this study we can hypothesize that the large variations observed in the affinities of Phe7 substituted analogs of SP must come from steric hindrance in the S7 binding site, which drastically restricts the space filling around the C $\alpha$ -C $\beta$  bond of residue 7.

L34 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:366335 HCAPLUS

DOCUMENT NUMBER: 125:55785

TITLE: Use of conformationally constrained peptides for a topographical analysis of the combining site of a monoclonal anti-substance P antibody

AUTHOR(S): Dery, O.; Josien, H.; Grassi, J.; Chassaing, G.; Couraud, J. Y.; Lavielle, S.

CORPORATE SOURCE: Serv. Pharmacologie Immunologie, CEA, Gif-sur-Yvette, 91191, Fr.

SOURCE: Biopolymers (1996), 39(1), 67-74

CODEN: BIPMAA; ISSN: 0006-3525

PUBLISHER: Wiley

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The topog. of the binding site of a monoclonal anti-substance P antibody directed toward the C-terminal pentapeptide of substance P, Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH<sub>2</sub>, was analyzed further using a wide range of constrained analogs of substance P. Results obtained in the present study show the following: (a) The binding subsites of Phe7 and Phe8 are large and deep, accommodating various side chains, including nonarom. amino acids. (B) In contrast, the binding pockets for Gly-Leu-Met-NH<sub>2</sub> appear more restrictive. Consequently, five residues in the peptide are necessary for the high binding affinity to the antibody, the C-terminal tripeptide determining the binding specificity. These data, which appear to contradict those previously published, illustrate the limits of conclusions drawn from studies generally carried out using exclusively Ala-substituted peptides. In addition, the present results indicate that the topog. of the binding site of this monoclonal antibody differs from that of the specific substance P neurokinin-1 receptor, in agreement with the differences observed in the fine specificities of these two substance P binding macromols.

L34 ANSWER 33 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:48103 HCAPLUS

DOCUMENT NUMBER: 124:176598

TITLE: Cascade radical reactions of isonitriles: a second-generation synthesis of (20S)-camptothecin, topotecan, irinotecan, and GI-147211C

AUTHOR(S): Curran, Dennis P.; Ko, Sung-Bo; Josien, Hubert

CORPORATE SOURCE: Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260, USA

SOURCE: Angewandte Chemie, International Edition in English (1996), Volume Date 1995, 34(23/24), 2683-4

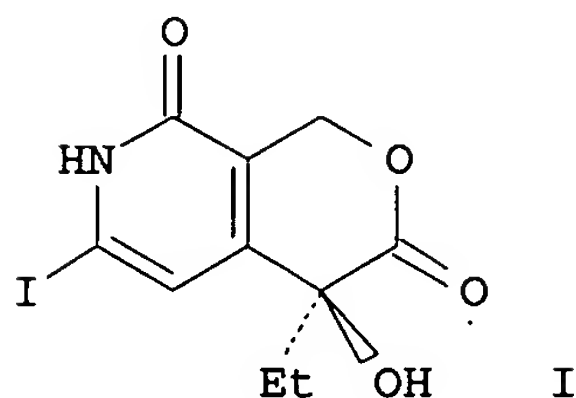
CODEN: ACIEAY; ISSN: 0570-0833

PUBLISHER: VCH

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S) : CASREACT 124:176598  
GI



AB A highly convergent second-generation synthesis of the title compds was achieved from 2-bromo-6-methoxypyridine via the lactone I, which was combined with propargyl bromides and aryl isonitriles in as few as two steps.

L34 ANSWER 34 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1995:978013 HCAPLUS  
DOCUMENT NUMBER: 124:145849  
TITLE: Selective N-functionalization of 6-substituted-2-pyridones  
AUTHOR(S): Liu, Hui; Ko, Sung-Bo; Josien, Hubert; Curran, Dennis P.  
CORPORATE SOURCE: Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260, USA  
SOURCE: Tetrahedron Letters (1995), 36(49), 8917-20  
CODEN: TELEAY; ISSN: 0040-4039  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 124:145849

AB 6-Substituted-2-pyridones can be selectively N-alkylated by treatment with NaH/LiBr in a mixture of DMF and DME. Yields of N-propargylated, N-allylated, and other N-functionalized products are good, and only small amts. of the isomeric O-alkylated product (<10%) are typically formed. The sodium hydride/lithium bromide-mediated propargylation of 6-bromo-2-pyridone with propargyl bromide gave 141807503 (84% yield).

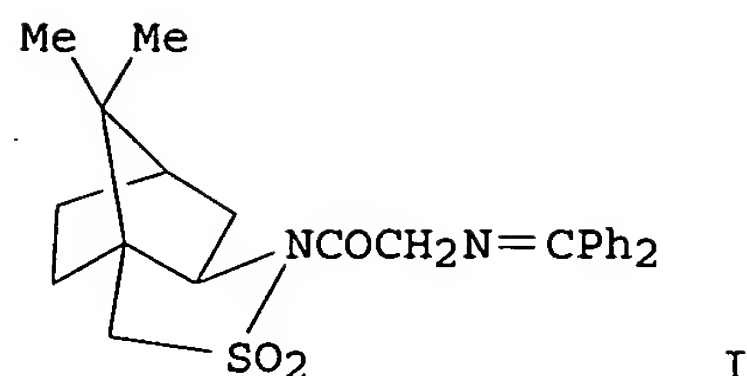
L34 ANSWER 35 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1994:316363 HCAPLUS  
DOCUMENT NUMBER: 120:316363  
TITLE: Design and Synthesis of Side-Chain Conformationally Restricted Phenylalanines and Their Use for Structure-Activity Studies on Tachykinin NK-1 Receptor  
AUTHOR(S): Josien, Hubert; Lavielle, Solange; Brunissen, Alie; Saffroy, Monique; Torrens, Yvette; Beaujouan, Jean-Claude; Glowinski, Jacques; Chassaing, Gerard  
CORPORATE SOURCE: Laboratoire de Chimie Organique Biologique, Universite P. et M. Curie, Paris, 75005, Fr.  
SOURCE: Journal of Medicinal Chemistry (1994), 37(11), 1586-601  
CODEN: JMCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Constrained analogs of phenylalanine have been conceptually designed for



analyzing the binding pockets of Phe7 (S7) and Phe8 (S8), two aromatic residues important for the pharmacol. properties of substance P (SP), i.e., L-tetrahydroisoquinoline-2-carboxylic acid, L-diphenylalanine, L-9-fluorenylglycine (Flg), 2-indanylglycine, the diastereomers of L-1-indanylglycine (Ing) and L-1-benz[f]indanylglycine (Bfi), and the Z and E isomers of dehydrophenylalanine ( $\Delta$ ZPhe,  $\Delta$ EPhe). Binding studies were performed with appropriate ligands and tissue preps. allowing the discrimination of the three tachykinin binding sites, neurokinin-1 (NK-1), NK-2, and NK-3. The potencies of these agonists were evaluated in the guinea pig ileum bioassay. According to the binding data, it is concluded that the S7 subsite is small, as only the gauche (-) probe [(2S,3S)-Ing7]SP presents a high affinity for specific NK-1 binding sites. Surprisingly, the [ $\Delta$ EPhe7]SP analog, which projects the aromatic ring toward the trans orientation, is over 40-fold more potent than the Z isomer, [ $\Delta$ ZPhe7]SP. A plausible explanation of these conflictual results is that either the binding protein quenches the minor trans rotamer of [(2S,3S)-Ing7]SP in solution or this constrained amino acid side chain rotates when inserted in the protein. In position 8, the high binding affinities of [Flg8]SP and [(2S,3S)-Bfi8]SP suggest that the S8 subsite is large enough to accept two aromatic rings in the gauche (-) and one aromatic ring in the trans direction. Peptides bearing two conformational probes in positions 7, 8, or 9 led to postulate that S7, S8, and S9 subsites are independent from each other. The vols. available for side chains 7 and 8 are estimated as close to 110 and 240 Å<sup>3</sup>, resp. The large volume of the S8 subsite raises question on the localization of the SP-binding site in the NK-1 receptor. If SP were to bind in the transmembrane domains, the cleft defined by the 7 transmembrane segments must rearrange during the binding process in order to bind a peptide in an  $\alpha$ -helical structure and at least one large binding subsite in position 8. Thus, indirect topog. anal. with constrained amino acids might contribute to the anal. of the receptor/ligand dynamics. Finally, this study demonstrates that a good knowledge of the peptide backbone structure and a combination of constrained amino acids are prerequisites to confidently attribute the preferred orientation(s) of an amino acid side chain.

L34 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1993:102419 HCAPLUS  
 DOCUMENT NUMBER: 118:102419  
 TITLE: Asymmetric synthesis of the diastereoisomers of  
 L-1-indanylglycine and L-1-benz[f]indanylglycine,  
 $\chi$ 1, $\chi$ 2-constrained side-chain derivatives of  
 L-phenylalanine and L-2-naphthylalanine  
 AUTHOR(S): **Josien, Hubert**; Chassaing, Gerard  
 CORPORATE SOURCE: Lab. Chim. Org. Biol., Univ. Pierre-et-Marie Curie,  
 Paris, Fr.  
 SOURCE: Tetrahedron: Asymmetry (1992), 3(11), 1351-4  
 CODEN: TASYE3; ISSN: 0957-4166  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 118:102419  
 GI



AB The diastereoisomers of the title compds., novel topog. tools and analogs of phenylalanine and 2-naphthylalanine, were synthesized from sultam-derived glycine imine synthon I alkylated by judicious electrophiles, and subsequent hydrolysis and sultam-cleavage. An x-ray anal. on one alkylation product established the  $\beta$ -configuration.

L34 ANSWER 37 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:235112 HCAPLUS

DOCUMENT NUMBER: 116:235112

TITLE: A general synthesis of 1-nitro-2-phenyl-4-oxospiro[2.5]octanes

AUTHOR(S): Dauzonne, Daniel; Josien, Hubert; Demerseman, Pierre

CORPORATE SOURCE: Serv. Chim., Inst. Curie, Paris, F-75231, Fr.

SOURCE: Synthesis (1992), (3), 309-14

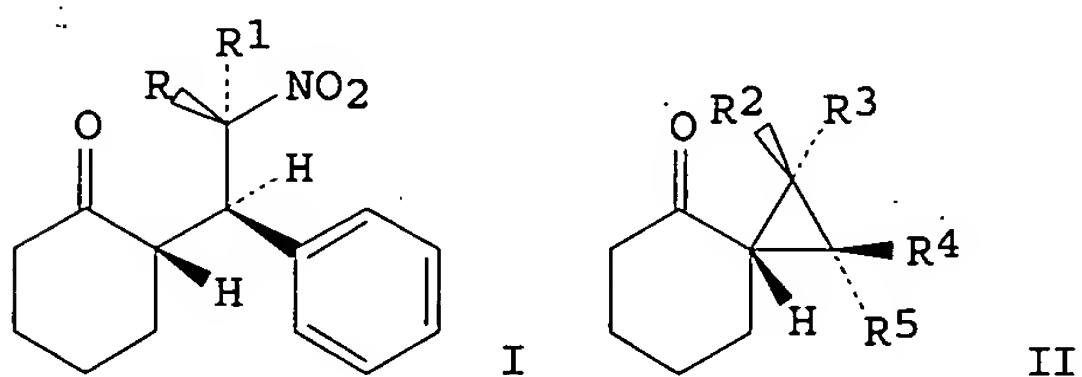
CODEN: SYNTBF; ISSN: 0039-7881

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 116:235112

GI



AB The title compds. were prepared by a facile two-step route starting from (2-chloro-2-nitroethyl)benzene and 1-morpholino-1-cyclohexene via the base-induced cyclopropanations of the intermediate 2-(2-chloro-2-nitro-1-phenylethyl)cyclohexanones. Michael addition reaction of 1-morpholino-1-cyclohexene with (2-chloro-2-nitroethenyl)benzene gave only a pair of diastereomeric 2-(2-chloro-2-nitro-1-phenylethyl)cyclohexanones I (R = Cl, R1 = H) and I (R = H, R1 = Cl) in 92% overall yield and in a 62:38 diastereomer ratio, resp. Cyclopropanation of I (R = Cl, R1 = H) and I (R = H, R1 = Cl) gave 1-nitro-2-phenyl-4-oxospiro[2.5]octanes II (R2 = H; R3 = NO2, R4 = Ph, R5 = H) in 53% yield and II (R2 = NO2; R3 = H, R4 = H, R5 = Ph) in 40% yield.

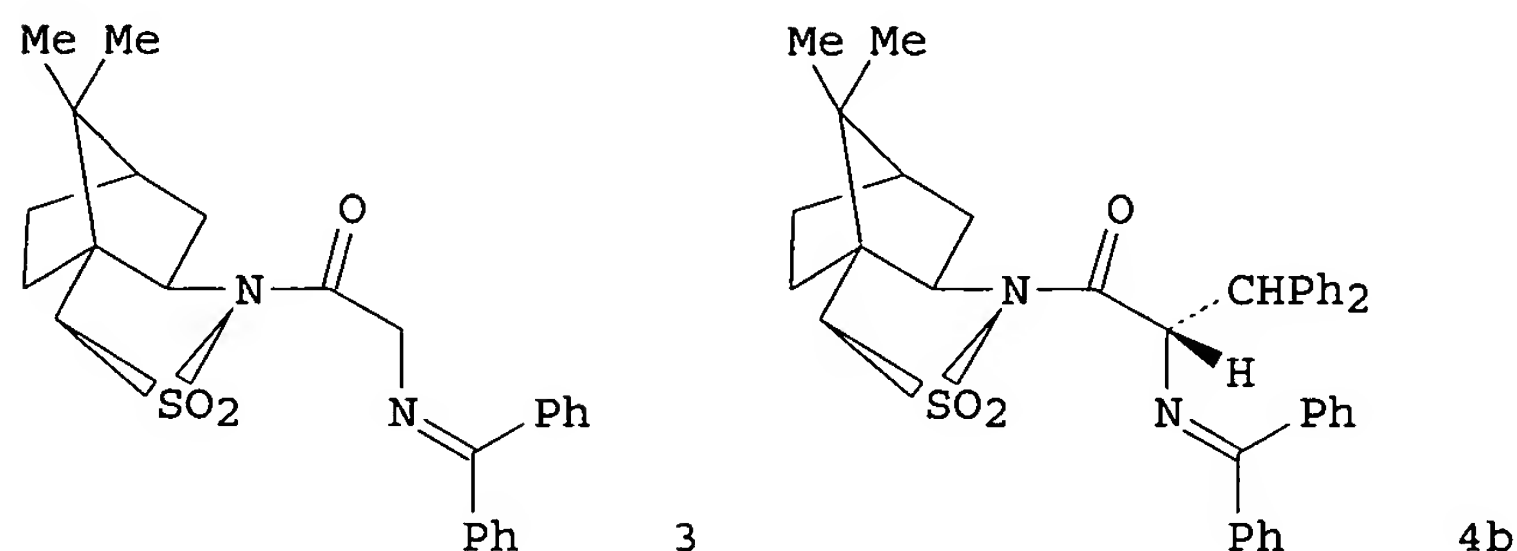
L34 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:84146 HCAPLUS

DOCUMENT NUMBER: 116:84146

TITLE: Asymmetric synthesis of L-diphenylalanine and L-9-fluorenylglycine via room temperature alkylations

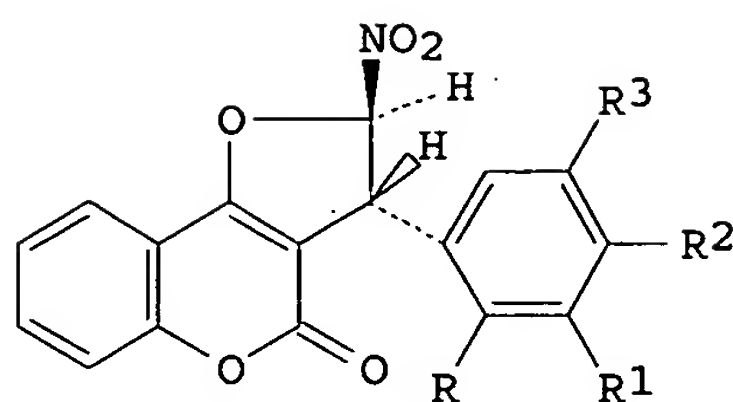
AUTHOR(S): of a sultam-derived glycine imine  
**Josien, Hubert**; Martin, Arnaud; Chassaing, Gerard  
 CORPORATE SOURCE: Lab. Chim. Org. Biol., Univ. Pierre et Marie Curie, Paris, Fr.  
 SOURCE: Tetrahedron Letters (1991), 32(45), 6547-50  
 CODEN: TELEAY; ISSN: 0040-4039  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 116:84146  
 GI



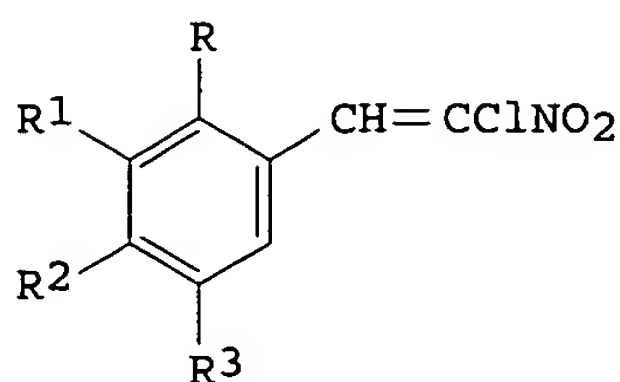
AB L-Diphenylalanine and L-9-fluorenylglycine were prepared from a sultam-derived glycine imine 3 via room temperature-asym.-alkylation/hydrolysis/mild-sultam-cleavage. The L-configuration was ascertained using an x-ray anal. of the alkylation product 4b.

L34 ANSWER 39 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1991:164057 HCAPLUS  
 DOCUMENT NUMBER: 114:164057  
 TITLE: (2-Chloro-2-nitroethenyl)benzenes as synthons: a general method for the preparation of 2,3-dihydro-2-nitro-3-phenyl-4H-furo[3,2-c][1]benzopyran-4-ones and 3-phenyl-4H-furo[3,2-c][1]benzopyran-4-ones  
 AUTHOR(S): Dauzone, Daniel; **Josien, Hubert**; Demerseman, Pierre  
 CORPORATE SOURCE: Serv. Chim., Inst. Curie, Paris, F75231, Fr.  
 SOURCE: Tetrahedron (1990), 46(21), 7359-71  
 CODEN: TETRAB; ISSN: 0040-4020  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 114:164057  
 GI

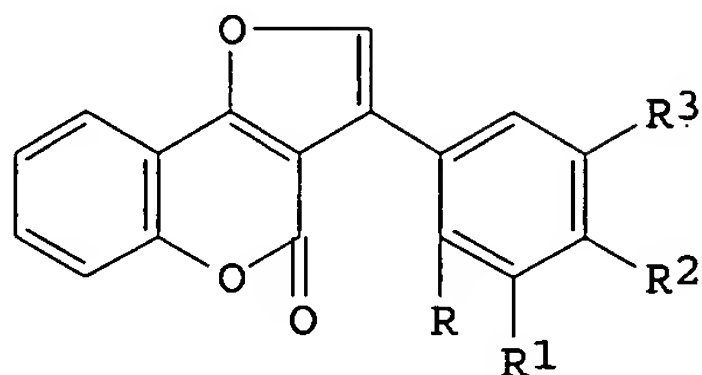




I



II



III

AB A convenient and general method for the preparation of dihydronitrophenylfurobenzopyranones (I; R, R1, R2 = H, Cl, NO2, OMe; R3 = H, OMe) from 4-hydroxycoumarin and (chloronitroethenyl)benzenes (II) in the presence of KF is described. By replacing KF in the above reaction with Et3N the hitherto unknown phenylfurobenzopyranones (III) are obtained in a one-pot process.

L34 ANSWER 40 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:102796 HCAPLUS

DOCUMENT NUMBER: 114:102796

TITLE: Synthesis of conformationally constrained phenylalanines and their incorporation into tachykinins

AUTHOR(S): Chassaing, G.; Josien, H.; Lavielle, S.

CORPORATE SOURCE: Lab. Chim. Org. Biol., Univ. Paris VI, Paris, F-75005, Fr.

SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 11th (1990), Meeting Date 1989, 935-6. Editor(s): Rivier, Jean E.; Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth. CODEN: 56XTA7

DOCUMENT TYPE: Conference

LANGUAGE: English

AB A symposium report on the synthesis of title phenylalanines, e.g. fluorenylglycine and diphenylalanine, and their incorporation into tachykinins.

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L4 STR

Ak~Cy	Ak~O~Ak	G1~Hy~SO2Cy
@10 11	@12 13 14	16 15 8 9

VAR G1=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/10/12

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

GGCAT IS MCY AT 15

DEFAULT ECLEVEL IS LIMITED

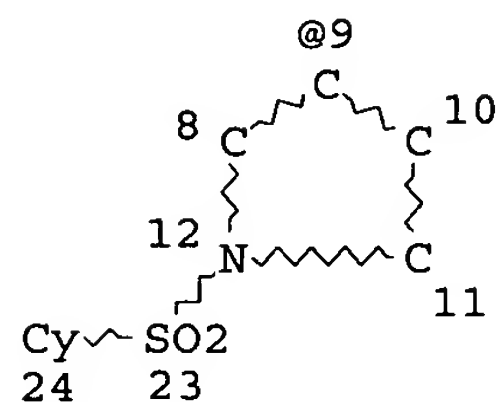
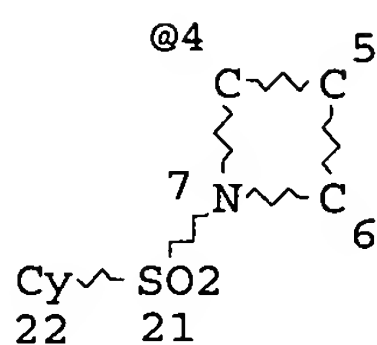
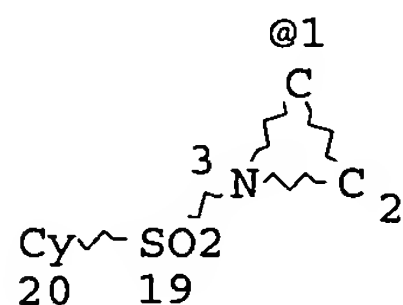
GRAPH ATTRIBUTES:

RSPEC I

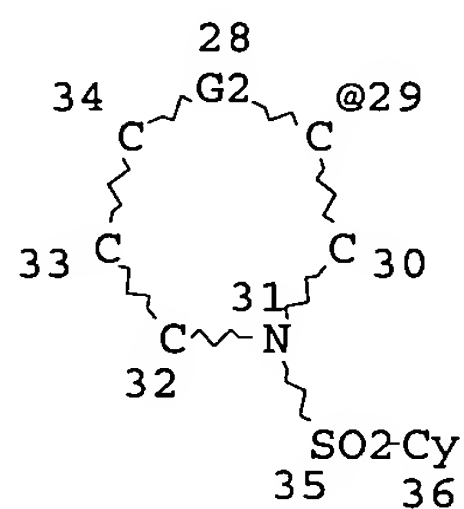
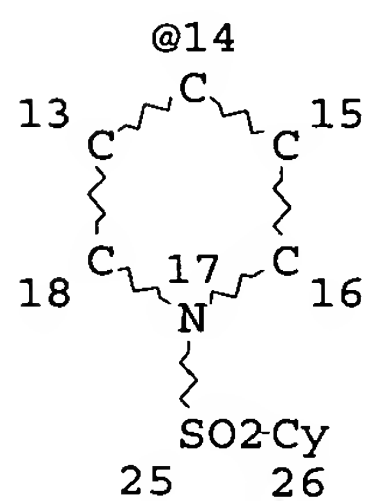
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE

L10 STR



G1 27



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REP G2=(1-5) C

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

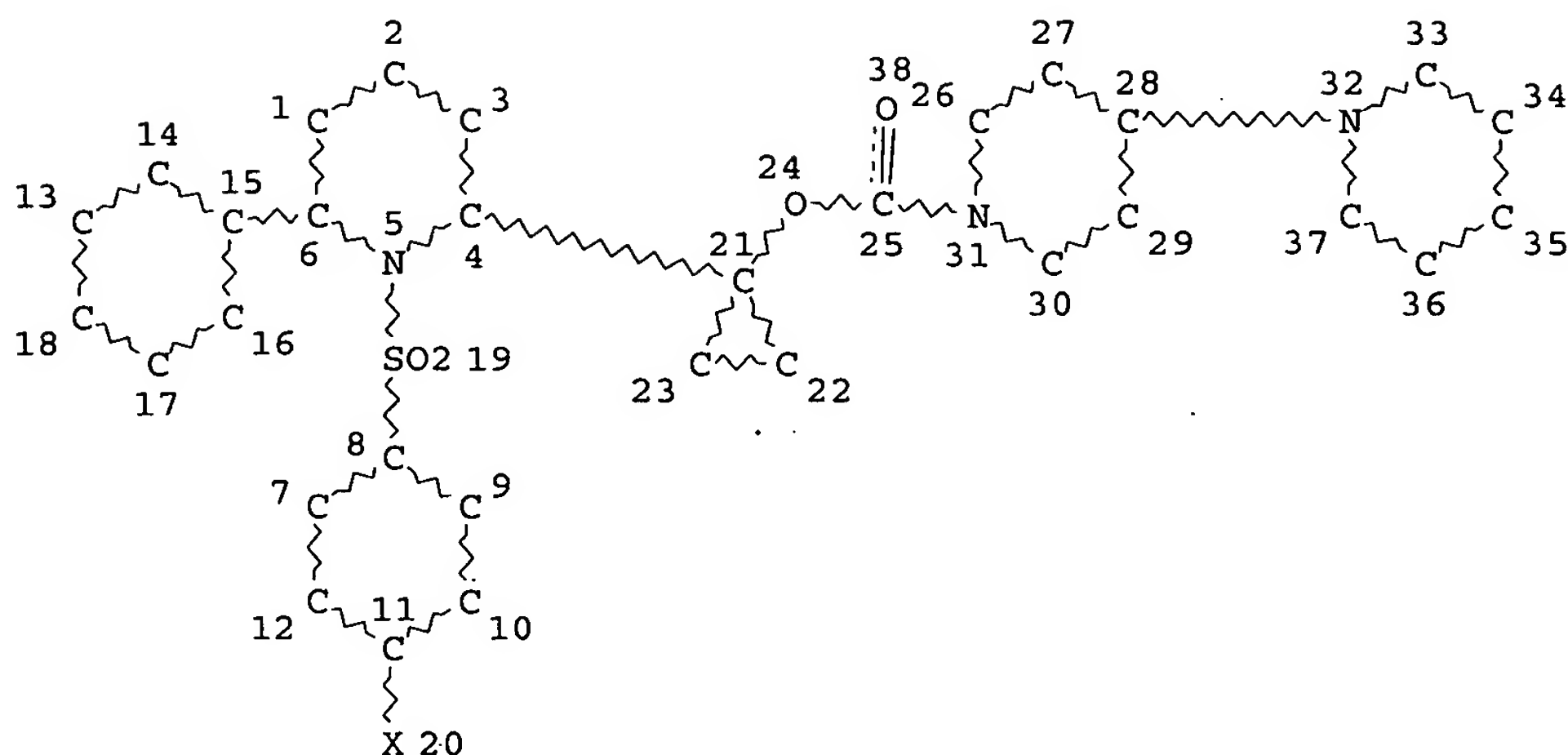
RSPEC I

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L12 25437 SEA FILE=REGISTRY SSS FUL L4 AND L10

L13 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE

L15 5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13  
L16 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15  
L17 25432 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15  
L18 183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE  
L19 3443 SEA FILE=HCAPLUS ABB=ON PLU=ON L17  
L20 2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?  
L21 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND L20  
L22 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L16  
L23 450 SEA FILE=HCAPLUS ABB=ON PLU=ON L19(L) INHIBIT?  
L24 372 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND PD=<DECEMBER 8, 2003  
L25 301 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND PATENT/DT  
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L35 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:331941 HCAPLUS

TITLE: Optimization of purine based PDE1/PDE5 inhibitors to a potent and selective PDE5 inhibitor for the treatment

of male ED  
AUTHOR(S): Boyle, Craig D.; Xu, Ruo; **Asberom, Theodros**;  
Chackalamannil, Samuel; Clader, John W.; Greenlee,  
William J.; Guzik, Henry; Hu, Yuequing; Hu, Zhiyong;  
Lankin, Claire M.; Pissarnitski, Dmitri A.; Stamford,  
Andrew W.; Wang, Yuguang; Skell, Jeffrey; Kurowski,  
Stanley; Vemulapalli, Subbarao; Palamanda, Jairam;  
CORPORATE SOURCE: Chintala, Madhu; Wu, Ping; Myers, Joyce; Wang, Peng  
Schering-Plough Research Institute, Kenilworth, NJ,  
07033, USA  
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005),  
15(9), 2365-2369  
CODEN: BMCLE8; ISSN: 0960-894X  
PUBLISHER: Elsevier B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB In search of a PDE5 inhibitor for erectile dysfunction, an SAR was  
developed from a PDE1/PDE5 purine series of leads, which had modest PDE5  
potency and poor isoenzyme selectivity. A compound (41) with PDE5  
inhibition and in vivo activity similar to sildenafil was discovered from  
this effort. In addition, purine 41 demonstrated superior overall PDE  
isoenzyme selectivity when compared to the approved PDE5 inhibitors  
sildenafil, vardenafil, and tadalafil, which may result in a more  
favorable side-effect profile.

L35 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:226370 HCAPLUS  
TITLE: Discovery of a PDE5 inhibitor for the treatment of  
male ED  
AUTHOR(S): Boyle, Craig D.; Chackalamannil, Samuel; Lankin,  
Claire M.; Wang, Yuguang; Hu, Zhiyong; **Asberom,**  
**Theodros**; Clader, John W.; Greenlee, William J.;  
Guzik, Henry; Pissarnitski, Dmitri; Stamford, Andrew  
W.; Xu, Ruo; Skell, Jeffrey; Kurowski, Stanley;  
Vemulapalli, Subbarao; Palamanda, Jairam; Chintala,  
Mahdu; Wu, Ping; Myers, Joyce; Wang, Peng  
CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research  
Institute, Kenilworth, NJ, 07033, USA  
SOURCE: Abstracts of Papers, 227th ACS National Meeting,  
Anaheim, CA, United States, March 28-April 1, 2004  
(2004), MEDI-012. American Chemical Society:  
Washington, D. C.  
CODEN: 69FGKM  
DOCUMENT TYPE: Conference; Meeting Abstract  
LANGUAGE: English  
AB Using a stepwise approach to improve upon the phys. and pharmacol.  
properties of a xanthine lead structure, we discovered a PDE5 inhibitor  
for the treatment of male ED. This compound improves upon the PDE isoenzyme  
selectivity, enzyme inhibition, and PK profile of the leading drug on the  
market, sildenafil (Viagra). This paper will summarize the medicinal  
chemical effort toward the discovery of potent and selective PDE5 inhibitors.

L35 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:153600 HCAPLUS  
DOCUMENT NUMBER: 140:350038  
TITLE: SAR development of polycyclic guanine derivatives  
targeted to the discovery of a selective PDE5  
inhibitor for treatment of erectile dysfunction  
AUTHOR(S): Pissarnitski, Dmitri A.; **Asberom, Theodros**;  
Boyle, Craig D.; Chackalamannil, Samuel; Chintala,

CORPORATE SOURCE: Madhu; Clader, John W.; Greenlee, William J.; Hu, Yueqing; Kurowski, Stanley; Myers, Joyce; Palamanda, Jairam; Stamford, Andrew W.; Vemulapalli, Subbarao; Wang, Yuguang; Wang, Peng; Wu, Ping; Xu, Ruo  
Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(5), 1291-1294  
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Development of structure-activity relationship of cyclic guanines I lead us to discovery of a potent and selective series of phosphodiesterase 5 inhibitors 52-59 (IC<sub>50</sub>=1.3-11.0 nM, PDE6/5=116-600).

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:634975 HCAPLUS

TITLE: Discovery of Sch 444877, a potent, selective and orally active cyclic guanine PDE5 inhibitor

AUTHOR(S): Wang, Yuguang; Chackalamannil, Samuel; Stamford, Andrew; Boyle, Craig D.; Hu, Zhiyong; Lankin, Claire; Clader, John; Xu, Ruo; **Asberom, Theodros**; Pissarnitski, Dmitri; Greenlee, William; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Mahdu; Wu, Ping; Myers, Joyce; Wang, Peng

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), MEDI-367. American Chemical Society: Washington, D. C.  
CODEN: 69EKY9

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Sch 444877 is a tricyclic guanine derived potent inhibitor of human PDE5 isoenzyme with an IC<sub>50</sub> value of 1.5 nM. Its PDE6/PDE5 selectivity is about 250-fold. In the dog pelvic nerve stimulation model, Sch 444877 dose-dependently increased cavernosal pressure with an ED<sub>100</sub> slightly more potent than sildenafil. It also showed a rapid onset and fast clearance PK profile.

L35 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:396889 HCAPLUS

DOCUMENT NUMBER: 138:401744

TITLE: Preparation of polycyclic guanine derivative phosphodiesterase V inhibitors

INVENTOR(S): **Asberom, Theodros**; Clader, John W.; Hu, Yueqing; Pissarnitski, Dmitri A.; Stamford, Andrew W.; Xu, Ruo

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 95 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042216	A1	20030522	WO 2002-US35721	20021107
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US 2003176413	A1	20030918	US 2002-290011	20021107
EP 1442042	A1	20040804	EP 2002-786685	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005509038	T2	20050407	JP 2003-544052	20021107
PRIORITY APPLN. INFO.:			US 2001-344498P	P 20011109
			WO 2002-US35721	W 20021107
OTHER SOURCE(S):		MARPAT 138:401744		
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y = alkyl, aryl] are prepared For instance, 4-amino-1-benzyl-5-(ethoxycarbonyl)imidazole (preparation given) is treated with ethylisocyanate (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe, reflux, 4 h), subsequently treated with POCl<sub>3</sub> and the product used to alkylate (R)-2-amino-3-phenylpropanol (NMP, 130°, 12 h) which provides II. II is treated with MsCl (Et<sub>3</sub>N), debenzylated (MeOH, NH<sub>4</sub>O<sub>2</sub>CH, Pd(OH)<sub>2</sub>/C, reflux, 3 h), brominated (HOAc, NaOAc, Br<sub>2</sub>), alkylated with 3-chloro-4-methoxybenzyl bromide (DMF, K<sub>2</sub>CO<sub>3</sub>) and treated with NaOEt (DMF/EtOH) to afford III. III has IC<sub>50</sub> < 4.1 nM for PDE V and IC<sub>50</sub> > 300 nM for PDE VI. I are useful for treating sexual dysfunction.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:202642 HCAPLUS

DOCUMENT NUMBER: 138:238193

TITLE: Preparation of polycyclic guanines for therapeutic use as phosphodiesterase V inhibitors

INVENTOR(S): **Asberom, Theodros**; Hu, Yueqing;  
 Pissarnitski, Dmitri A.; Xu, Ruo; Wang, Yuguang;  
 Chackalamannil, Samuel; Clader, John W.; Stamford, Andrew W.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 179 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

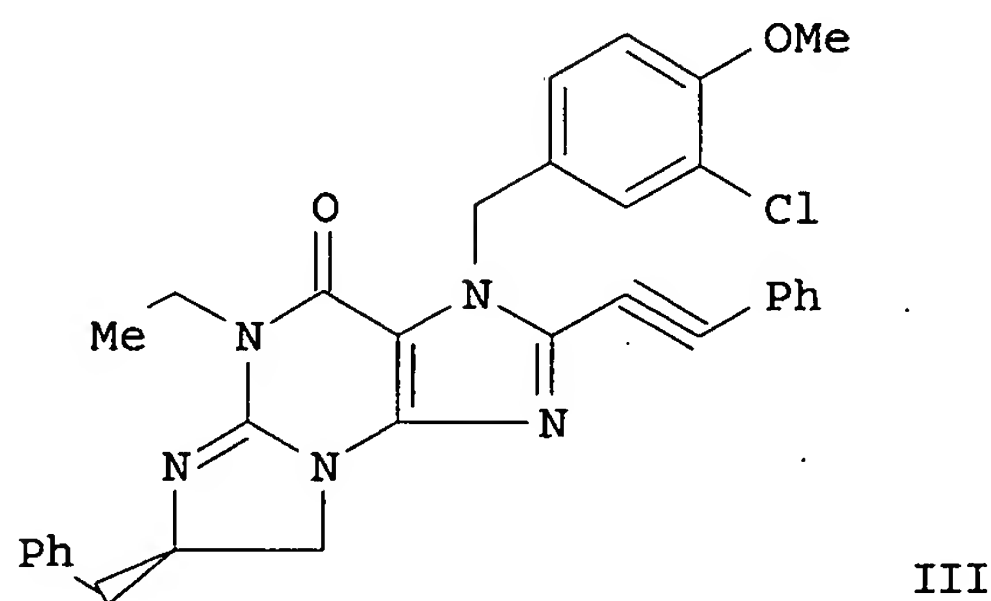
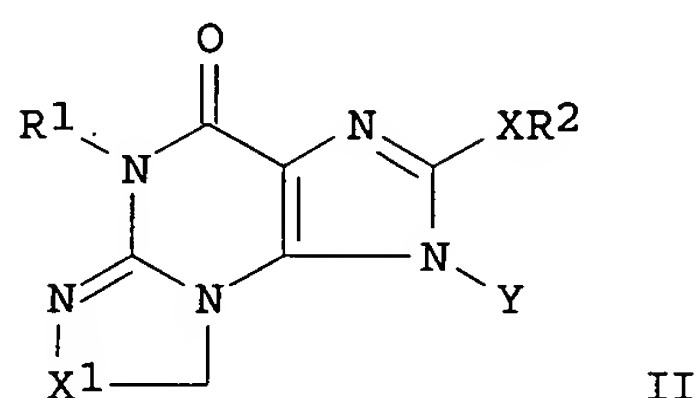
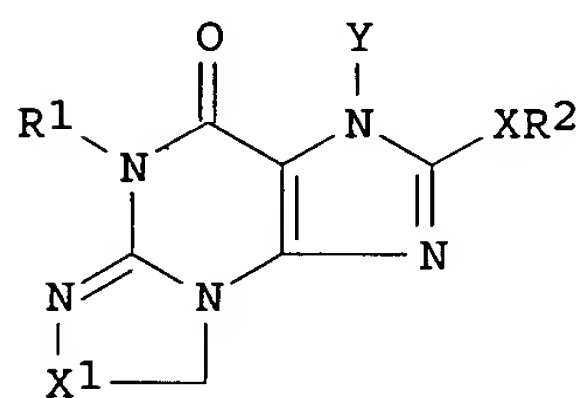
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003020724	A1	20030313	WO 2002-US27181	20020826
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CA 2457944	AA	20030313	CA 2002-2457944	20020826
US 2003153587	A1	20030814	US 2002-227778	20020826
EP 1421084	A1	20040526	EP 2002-761506	20020826
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JP 2005502684	T2	20050127	JP 2003-524994	20020826
PRIORITY APPLN. INFO.:			US 2001-315395P	P 20010828
			WO 2002-US27181	W 20020826

OTHER SOURCE(S): MARPAT 138:238193

GI



AB Purine cyclic derivs., such as I and II [R1 = H, alkyl, cycloalkyl; R2 = N3, CN, oximino, halo, haloalkyl, cycloalkenyl, heteroaryl, etc.; R3 = H, alkyl, arylalkyl, etc.; X = bond, connecting group, such as O, S, SO, SO2, amino, etc.; X1 = (CH2)2, CHR3, etc.; Y = H, alkyl, arylalkyl, etc.], were prepared for pharmaceutical use as phosphodiesterase V (PDE5) inhibitors. These polycyclic guanines are useful for treatment of physiol. disorders, wherein the physiol. disorder, symptom or disease is urogenital, such as male erectile dysfunction, peripheral vascular, angina pectoris, restenosis post angioplasty, endarterectomy, stent introduction, cerebral stroke, respiratory tract, allergic associated with atopy, pulmonary



hypertension, ischemic heart, impaired glucose tolerance, diabetes, neuropathy, insulin resistance syndrome, hyperglycemia, polycystic ovarian syndrome, glomerular renal insufficiency, nephritis, tubular interstitial, autoimmune, glaucoma, intestinal motility, cachexia, cancer, cognitive impairment or nutcracker esophageal. Thus, polycyclic guanine III was prepared via a multistep synthetic sequence which included cyclization of (R)-2-amino-3-phenyl-1-propanol with 2-chloro-1-ethyl-1,7-dihydro-7-(phenylmethyl)-6H-purin-6-one to form the desired cyclic guanine ring, followed sequentially by removal of the benzyl group using Pd(OH)<sub>2</sub>/C in MeOH, 8-bromination using Br<sub>2</sub> and NaOAc, 7-benylation with 3-chloro-4-methoxybenzyl bromide using K<sub>2</sub>CO<sub>3</sub> in DMF, and finally, alkynylation with phenylacetylene using (PPh<sub>3</sub>)<sub>2</sub>PdCl<sub>2</sub>, CuI and Et<sub>3</sub>N. The prepared polycyclic guanines were assayed for inhibition of PDE5 activity.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:767305 HCAPLUS

DOCUMENT NUMBER: 138:331192

TITLE: Design and synthesis of xanthine analogues as potent and selective PDE5 inhibitors

AUTHOR(S): Wang, Yuguang; Chackalamannil, Samuel; Hu, Zhiyong; Boyle, Craig D.; Lankin, Claire M.; Xia, Yan; Xu, Ruo; **Asberom, Theodros**; Pissarnitski, Dmitri; Stamford, Andrew W.; Greenlee, William J.; Skell, Jeffrey; Kurowski, Stanley; Vemulapalli, Subbarao; Palamanda, Jairam; Chintala, Madhu; Wu, Ping; Myers, Joyce; Wang, Peng

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(21), 3149-3152

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have discovered potent and selective xanthine PDE5 inhibitors. One compound (PDE5 IC<sub>50</sub>=0.6 nM, PDE6/PDE5=101) demonstrated similar functional efficacy and pharmacokinetic profile to sildenafil (PDE5 IC<sub>50</sub>=3.5 nM, PDE6/PDE5=7).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:136921 HCAPLUS

DOCUMENT NUMBER: 137:93725

TITLE: Synthesis and structure-Activity relationships of M2-Selective muscarinic receptor ligands in the 1-[4-(4-Arylsulfonyl)-phenylmethyl]-4-(4-piperidinyl)-piperazine family

AUTHOR(S): McCombie, Stuart W.; Lin, Sue-Ing; Tagat, Jayaram R.; Nazareno, Dennis; Vice, Susan; Ford, Jennifer; **Asberom, Theodros**; Leone, Daria; Kozlowski, Joseph A.; Zhou, Guowei; Ruperto, Vilma B.; Duffy, Ruth A.; Lachowicz, Jean E.

CORPORATE SOURCE: Department of Chemistry, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(5), 795-798

CODEN: BMCLE8; ISSN: 0960-894X



PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 137:93725

AB The synthesis and muscarinic binding properties of compds. based on the 1-[[4-(4-arylsulfonyl)phenyl]methyl]-4-(1-aroyl-4-piperidinyl)piperazine skeleton are described. For compds. substituted with appropriately configured Me groups at the benzylic center and at the piperazine 2-position, high levels of selective, M2 subtype affinity could be obtained, particularly when the terminal N-aroyl residue was ortho substituted.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:516896 HCAPLUS

DOCUMENT NUMBER: 135:282588

TITLE: Muscarinic agonists and antagonists in the treatment of Alzheimer's disease

AUTHOR(S): Greenlee, W.; Clader, J.; Asberom, T.; McCombie, S.; Ford, J.; Guzik, H.; Kozlowski, J.; Li, S.; Liu, C.; Lowe, D.; Vice, S.; Zhao, H.; Zhou, G.; Billard, W.; Binch, H.; Crosby, R.; Duffy, R.; Lachowicz, J.; Coffin, V.; Watkins, R.; Ruperto, V.; Strader, C.; Taylor, L.; Cox, K.

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA

SOURCE: Farmaco (2001), 56(4), 247-250

CODEN: FRMCE8; ISSN: 0014-827X

PUBLISHER: Elsevier Science S.A.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with refs. Alzheimer's disease (AD) is a neurodegenerative disease characterized by cognitive impairment and personality changes. The development of drugs for the treatment of the cognitive deficits of AD has focused on agents which counteract loss in cholinergic activity. Although symptoms of AD have been successfully treated with acetylcholinesterase inhibitors (tacrine, donepezil, rivastigmine, galanthamine), limited success has been achieved with direct M1 agonists, probably due to their lack of selectivity vs. other muscarinic receptor subtypes. Muscarinic M2 antagonists have been reported to increase synaptic levels of acetylcholine after oral administration to rats (e.g. BIBN-99, SCH-57790), but their selectivity vs. other muscarinic receptor subtypes is modest. Exploration of a series of piperidinylpiperidines has yielded the potent and selective M2 antagonist SCH-217443. This antagonist has excellent bioavailability in rats and dogs and shows activity in a rat model of cognition.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:202249 HCAPLUS

TITLE: Discovery of potent, non-peptide thrombin receptor antagonists

AUTHOR(S): Chackalamannil, Samuel; Xia, Yan; Clasby, Martin; Greenlee, William; Doller, Dario; Eagen, Keith; Tsai, Hsingan; Asberom, Theodros; Lin, Yan; Czarniecki, Michael; Ahn, Ho-Sam; Foster, Carolyn; Boykow, George

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research

SOURCE: Institute, Kenilworth, NJ, 07033, USA  
 Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001)  
 MEDI-342  
 CODEN: 69FZD4  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal; Meeting Abstract  
 LANGUAGE: English  
 AB In addition to its key role in hemostasis and wound healing, thrombin activates specific cell surface receptors known as protease-activated receptors (PAR). Activation of thrombin receptor stimulates proliferative and proinflammatory processes in a variety of cell types and may have implications in thrombosis, atherosclerosis, and restenosis. As such, a thrombin receptor antagonist may have considerable utility in the treatment of these diseases. Since a thrombin receptor antagonist is specific for the cellular actions of thrombin and does not interfere with the coagulation cascade, such agents are likely to confer added safety margin with regard to hemorrhagic side effects. Through high throughput screening, we have identified 2-iminobenzimidazole derivs. as well as synthetic analogs of the natural product himbacine as thrombin receptor antagonists. Systematic SAR studies in these classes of compds. led to thrombin receptor antagonists with single digit-nanomolar IC50 values. These compds. inhibited thrombin as well as peptide agonist-induced human platelet aggregation in a dose-dependent manner.

L35 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:202070 HCAPLUS  
 TITLE: Discovery of SCH 211803: A potent and highly selective muscarinic M2 antagonist and a promising new approach to the treatment of alzheimer's disease

AUTHOR(S): **Asberom, Theodros**; Billard, William; Binch, Herbert; Clader, John W.; Cox, Kathleen; Crosby, Gordon; Duffy, Ruth A.; Ford, Jenifer; Greenlee, William; Guzik, Henry; Kozlowski, Joseph A.; Lachowicz, Jean E.; Li, Shengjian; Liu, Charles; Lowe, Derek; McCombie, Stuart; Ruperto, Vilma B.; Strader, Catherine; Taylor, Lisa A.; Vice, Susan; Zhao, Hongrong; Zhou, Guowei

CORPORATE SOURCE: CV/CNS Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001)  
 MEDI-169  
 CODEN: 69FZD4

PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal; Meeting Abstract  
 LANGUAGE: English

AB Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a profound cognitive impairment that progresses eventually to an inability to function independently and ultimately to death. One of the consistent findings in the brains of AD patients is loss of cholinergic neurons in the regions of the brain known to be involved in learning and memory. The cholinergic approach to treatment of AD involves counteracting this loss in cholinergic activity by pharmacol. intervention. One approach to improving cholinergic activity is to raise acetylcholine levels through the use cholinesterase inhibitors. These compds. have shown modest efficacy in the clinic due in part to dose-limiting side effects. Another approach to increasing acetylcholine levels is through inhibition of presynaptic muscarinic M2 receptors that control acetylcholine release. This approach has not been successful in the past due to the absence of

comps. that show sufficient selectivity vs. other muscarinic receptors. We now describe the discovery of a class of potent and highly selective muscarinic M2 antagonists typified by SCH 211803. These comps. show=100x selectivity for the M2 receptor vs. other muscarinic receptors and are active in animal models of cognition. They also show a preclin. profile that is indicative of a superior safety profile compared with cholinesterase inhibitors. Thus, this class of comps. represents a promising new approach to the treatment of AD.

L35 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:323253 HCAPLUS

DOCUMENT NUMBER: 132:334655

TITLE: preparation of himbacine analogs as thrombin receptor antagonists

INVENTOR(S): Chackalamannil, Samuel; Asberom, Theodros; Xia, Yan; Doller, Dario; Clasby, Martin C.; Czarniecki, Michael F.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: U.S., 161 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6063847	A	20000516	US 1998-197442	19981123
US 6326380	B1	20011204	US 2000-545720	20000407
PRIORITY APPLN. INFO.:			US 1997-66518P	P 19971125
			US 1998-197442	A3 19981123

OTHER SOURCE(S): MARPAT 132:334655

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\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

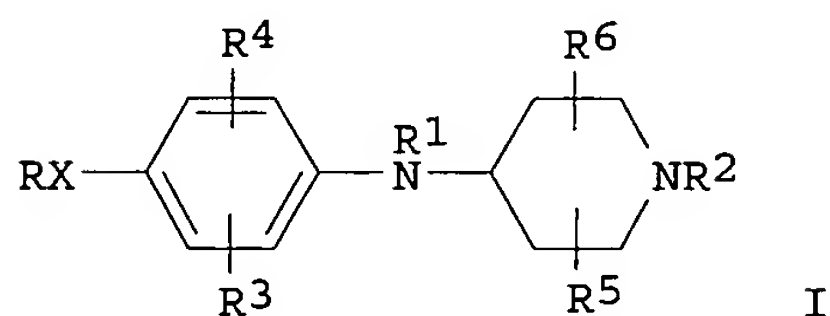
AB Heterocyclic-substituted tricyclics of the formula (I) [single dotted line represents an optional double bond; double dotted line represents an optional single bond; n = 0-2; Q = (un)substituted cycloalkyl, heterocycloalkyl, aryl or heteroaryl; Het = (un)substituted mono-, bi- or tricyclic heteroarom. group; B = -(CH<sub>2</sub>)<sub>n3</sub>-, wherein n<sub>3</sub> is 0-5, -CH<sub>2</sub>-O-, -CH<sub>2</sub>S-, -CH<sub>2</sub>-NR<sub>6</sub>-, -C(O)NR<sub>6</sub>-, -NR<sub>6</sub>C(O)-, etc.; X = -O- or -NR<sub>6</sub>- when the double dotted line represents a single bond, or X is -OH or -NHR<sub>20</sub> when the bond is absent; Y = =O, =S, (H, H), (H, OH) or (H, alkoxy) when the double dotted line represents a single bond, or when the bond is absent, Y = O, (H, H), (H, OH), (H, SH) or (H, C<sub>1</sub>-C<sub>6</sub> alkoxy); R<sub>15</sub> is absent when the double dotted line represents a single bond and is H, -NR<sub>18</sub>R<sub>19</sub>, or -OR<sub>17</sub> when the bond is absent; or Y = -O-(CH<sub>2</sub>)<sub>m</sub>-O- or -S-(CH<sub>2</sub>)<sub>m</sub>-S-, m = 1-2; and R<sub>15</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>19</sub> = H or alkyl, aryl etc.] or a pharmaceutically acceptable salt were synthesized. Thus (II) was prepared starting from (R)-3-butyn-2-ol and via condensation of fragment (III) and [5-[3-(trifluoromethyl)phenyl]-2-pyridinyl]methyl-phosphonic acid di-Et ester. II shows an IC<sub>50</sub> of 0.11 nM in in vitro thrombin receptor antagonist assay. Pharmaceutical comps. containing I as well as method of treating diseases associated with thrombosis, atherosclerosis, restenosis, hypertension, angina pectoris, arrhythmia, heart failure, and cancer are described.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1999:582651 HCAPLUS  
 DOCUMENT NUMBER: 131:214192  
 TITLE: Preparation of arylaminopiperidines as muscarinic M2 antagonists for treating memory loss  
 INVENTOR(S): Asberom, Theodros; Lowe, Derek B.; Green, Michael J.  
 PATENT ASSIGNEE(S): Schering Corporation, USA  
 SOURCE: U.S., 28 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5952349	A	19990914	US 1997-889486	19970708
PRIORITY APPLN. INFO.:			US 1996-21691P	P 19960710
OTHER SOURCE(S):	MARPAT	131:214192		

GI



AB Title compds. [I; X = bond, O, S, SO, SO<sub>2</sub>, CO, C(OR<sub>7</sub>)<sub>2</sub>, CH<sub>2</sub>O, CH:CH, CH<sub>2</sub>, CHA, CA<sub>2</sub>, CONR<sub>17</sub>, SO<sub>2</sub>NR<sub>17</sub>, etc.; R = cycloalkyl, (substituted) Ph, pyridyl, indolyl, quinolyl, etc.; R<sub>1</sub> = H, cyano, CF<sub>3</sub>, A, cycloalkyl, cycloalkenyl, alkenyl, COR<sub>15</sub>, CO<sub>2</sub>A, etc.; R<sub>2</sub> = cycloalkyl, cycloalkenyl, BOC, (substituted) 4-piperidiny], were prepared Thus, I (R = 3,4-methylenedioxyphenyl; X = SO<sub>2</sub>; R<sub>1</sub> = cyano; R<sub>2</sub> = cyclohexyl; R<sub>3</sub>-R<sub>6</sub> = H) showed K<sub>i</sub> = 0.44 nM for binding to M<sub>2</sub> receptors.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

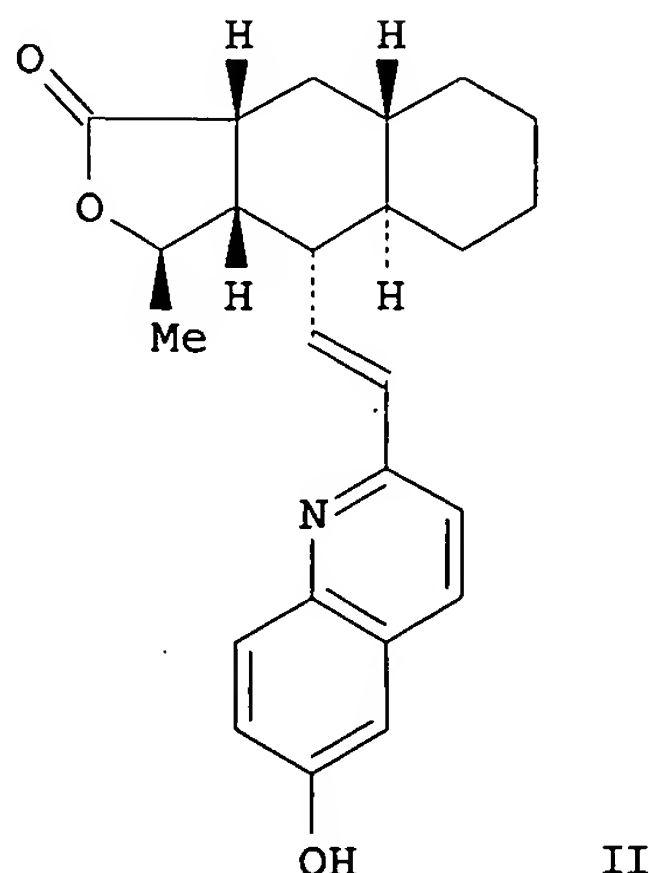
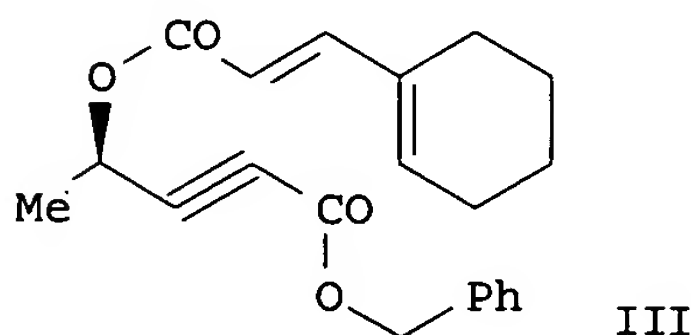
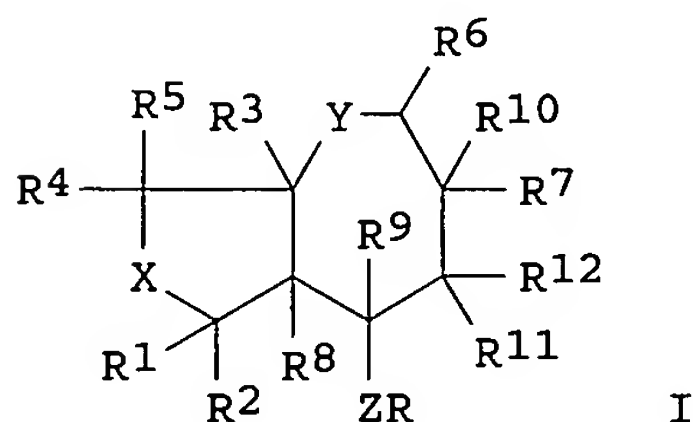
L35 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1999:355771 HCAPLUS  
 DOCUMENT NUMBER: 131:32085  
 TITLE: Preparation of himbacine analogs for use as thrombin receptor antagonists  
 INVENTOR(S): Chackalamannil, Samuel; Asberom, Theodros; Xia, Yan; Doller, Dario; Clasby, Martin C.; Czarniecki, Michael F.  
 PATENT ASSIGNEE(S): Schering Corporation, USA  
 SOURCE: PCT Int. Appl., 134 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926943	A1	19990603	WO 1998-US24523	19981123
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2309352	AA	19990603	CA 1998-2309352	19981123
CA 2309352	C	20050125		
AU 9914158	A1	19990615	AU 1999-14158	19981123
AU 747204	B2	20020509		
ZA 9810685	A	19991223	ZA 1998-10685	19981123
EP 1036072	A1	20000920	EP 1998-958039	19981123
EP 1036072	B1	20040506		
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TR 200001480	T2	20000921	TR 2000-200001480	19981123
BR 9812793	A	20001017	BR 1998-12793	19981123
JP 2001524479	T2	20011204	JP 2000-522101	19981123
JP 3449620	B2	20030922		
JP 2003128670	A2	20030508	JP 2002-315015	19981123
RU 2204557	C2	20030520	RU 2000-116548	19981123
IL 135797	A1	20030917	IL 1998-135797	19981123
AT 266025	E	20040515	AT 1998-958039	19981123
PT 1036072	T	20040831	PT 1998-958039	19981123
ES 2219919	T3	20041201	ES 1998-958039	19981123
NO 2000002659	A	20000724	NO 2000-2659	20000524
HK 1031726	A1	20040930	HK 2001-101899	20010316
PRIORITY APPLN. INFO.:			US 1997-977979	A 19971125
			JP 2000-522101	A3 19981123
			WO 1998-US24523	W 19981123

OTHER SOURCE(S):  
 GI

MARPAT 131:32085





AB Himbacine analogs I [R = heteroaryl, such as pyridinyl, quinolinyl, isoquinolinyl, etc.; R1, R2, R8, R10, R11 = H, alkyl, fluoroalkyl, cycloalkyl, alkenyl, aryl, heteroaryl, etc.; R3 = H, OH, alkoxy, alkylsulfinyl, alkylsulfonyl, alkyl, carboxyl, carbamido, aryl, etc.; R4, R5 = H, OH, alkyloxy, alkyl, amino, etc.; R4R5 = O, S; R6 = H; R6R10 = bond; R7R12 = fused alicyclic, fused aryl, fused heteroaryl, etc.; R9 = H, OH, alkoxy, halogen, haloalkyl; X = O, NR13; R13 = H, alkyl, Ph, etc.; Y = (CH2)n, n = 0 - 2; Z = connecting group, such as CH:CH, CH2CH2, CH2O, CH2S, CH2NH, CONH, etc.] were prepared for use as thrombin receptor antagonists for the treatment of diseases associated with thrombosis, atherosclerosis, restenosis, hypertension, angina pectoris, arrhythmia, heart failure, and cancer. Thus, lactone II was prepared starting from (R)-3-butyn-2-ol, trans-3-(1-cyclohexenyl)acrylic acid, and 6-hydroxyquinaldine via the formation and intramol. cycloaddn. of diester III. The prepared compds. were tested for thrombin receptor binding, platelet aggregation and antitumor activity.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:212795 HCAPLUS

DOCUMENT NUMBER: 130:267454

TITLE: Preparation of muscarinic antagonists

INVENTOR(S): Lowe, Derek B.; Chang, Wei K.; Kozlowski, Joseph A.; Berger, Joel G.; McQuade, Robert; Barnett, Allen; Sherlock, Margaret; Tom, Wing; Dugar, Sundeep; Chen, Lian-yong; Clader, John W.; Chackalamannil, Samuel; Wang, Yuguang; McCombie, Stuart W.; Tagat, Jayaram R.; Vice, Susan F.; Vaccaro, Wayne; Green, Michael J.; Browne, Margaret E.; **Asberom, Theodros**; Boyle, Craig D.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 602,403.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5889006	A	19990330	US 1996-700628	19960808
US 5883096	A	19990316	US 1996-602403	19960216
ZA 9601293	A	19960819	ZA 1996-1293	19960219
ZA 9707011	A	19980206	ZA 1997-7011	19970806
CA 2261725	AA	19980212	CA 1997-2261725	19970806
WO 9805292	A2	19980212	WO 1997-US13383	19970806
WO 9805292	A3	19980402		
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RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738999	A1	19980225	AU 1997-38999	19970806
AU 724001	B2	20000907		
EP 938483	A2	19990901	EP 1997-936296	19970806

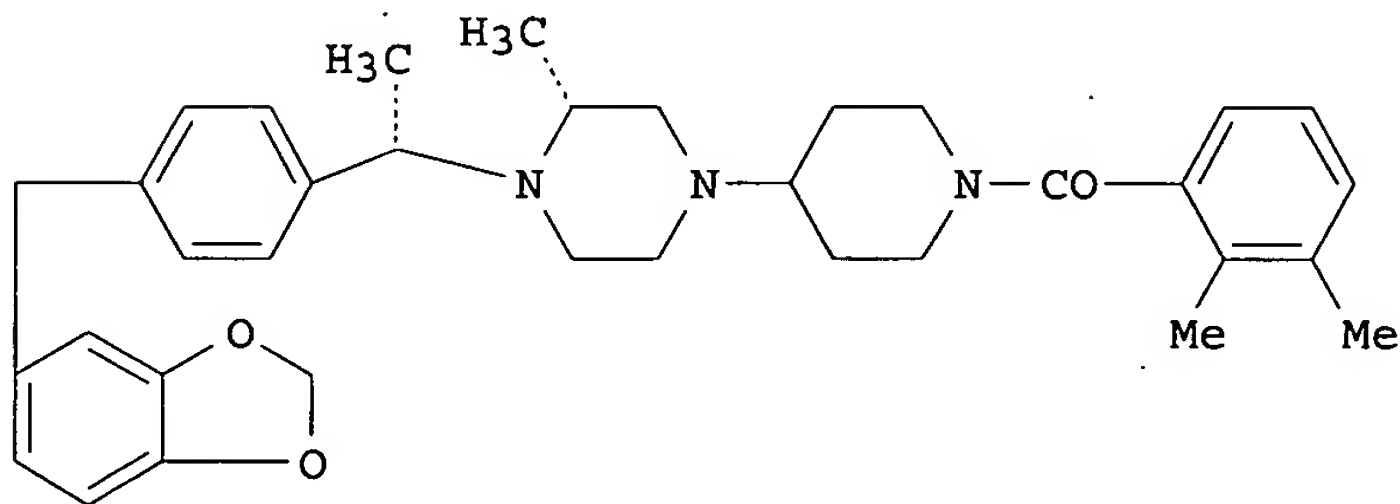
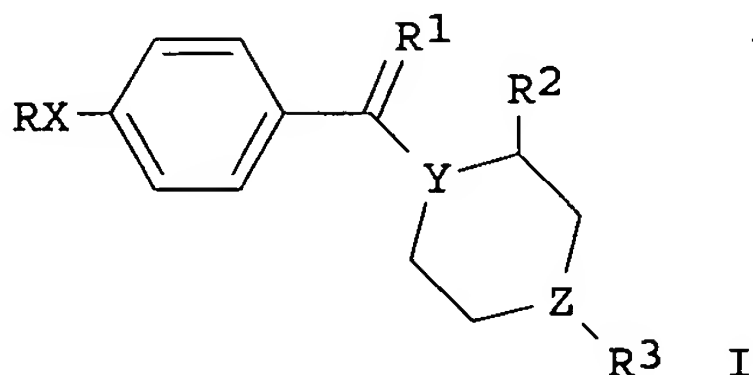
Ward 10\_663042-inventor search

EP 938483 B1 20030226  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,  
 LT, LV, FI, RO  
 CN 1232462 A 19991020 CN 1997-198479 19970806  
 CN 1084743 B 20020515  
 BR 9711119 A 19991123 BR 1997-11119 19970806  
 JP 2000501117 T2 20000202 JP 1998-508038 19970806  
 NZ 333801 A 20000428 NZ 1997-333801 19970806  
 AT 233260 E 20030315 AT 1997-936296 19970806  
 ES 2193391 T3 20031101 ES 1997-936296 19970806  
 NO 9900551 A 19990407 NO 1999-551 19990205  
 KR 2000029947 A 20000525 KR 1999-701175 19990208  
 US 6043255 A 20000328 US 1999-266079 19990310  
 HK 1018776 A1 20030829 HK 1999-103789 19990902

PRIORITY APPLN. INFO.:

US 1995-392697 B2 19950223  
 US 1995-457712 B2 19950602  
 US 1996-602403 A2 19960216  
 US 1996-700628 A 19960808  
 WO 1997-US13383 W 19970806

OTHER SOURCE(S): MARPAT 130:267454  
 GI



AB Di-N-substituted piperazine or 1,4 di-substituted piperadine compds. [I; Y = CH, N, C<sub>6</sub>H<sub>5</sub>C, CH<sub>3</sub>C, (CH<sub>3</sub>)<sub>2</sub>CHC, etc.; Z = N; X = O, S, SO<sub>2</sub>, NMe, CO, CH<sub>2</sub>; R = (un)substituted phenyl; R<sub>1</sub> = O, H<sub>2</sub>, Me and H, spiroheterocyclic; R<sub>2</sub> = Me, H; R<sub>3</sub> = 2-MeC<sub>6</sub>H<sub>4</sub>CO, COOEt, SO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, COCF<sub>2</sub>CF<sub>3</sub>, etc.] (including all isomers, salts, esters, and solvates) are prepared as muscarinic antagonists useful for treating cognitive disorders such as Alzheimer's disease. Pharmaceutical compns. and methods of preparation are also disclosed. Also disclosed are synergistic combinations of compds. of the above formula with acetylcholinesterase inhibitors. Thus, compound II was prepared from (S)-α-methylbenzylamine and trifluoroacetic anhydride via 12 steps.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:193839 HCAPLUS

DOCUMENT NUMBER: 130:252377

TITLE: Preparation of di-N-substituted piperazines or 1,4  
disubstituted piperidines as muscarinic antagonistsINVENTOR(S): Lowe, Derek; Chang, Wei; Kozlowski, Joseph; Berger,  
Joel G.; Mcquade, Robert; Barnett, Allen; Sherlock,  
Margaret; Tom, Wing; Dugar, Sundeep; Chen, Lian-Yong;  
Clader, John W.; Chackalamannil, Samuel; Yuguang,  
Wang; Mccombe, Stuart W.; Tagat, Jayaram R.; Vice,  
Susan F.; Vaccaro, Wayne; Green, Michael J.; Browne,  
Margaret E.; **Asberom, Theodros**

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 457,712,  
abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5883096	A	19990316	US 1996-602403	19960216
CA 2212895	AA	19960829	CA 1996-2212895	19960216
TW 464646	B	20011121	TW 1996-85101945	19960216
ES 2215190	T3	20041001	ES 1996-906286	19960216
ZA 9601293	A	19960819	ZA 1996-1293	19960219
US 5889006	A	19990330	US 1996-700628	19960808
US 6037352	A	20000314	US 1998-195742	19981119
US 6043255	A	20000328	US 1999-266079	19990310
US 6288068	B1	20010911	US 2000-482168	20000112
US 2002103205	A1	20020801	US 2001-902849	20010711
US 6498168	B2	20021224		

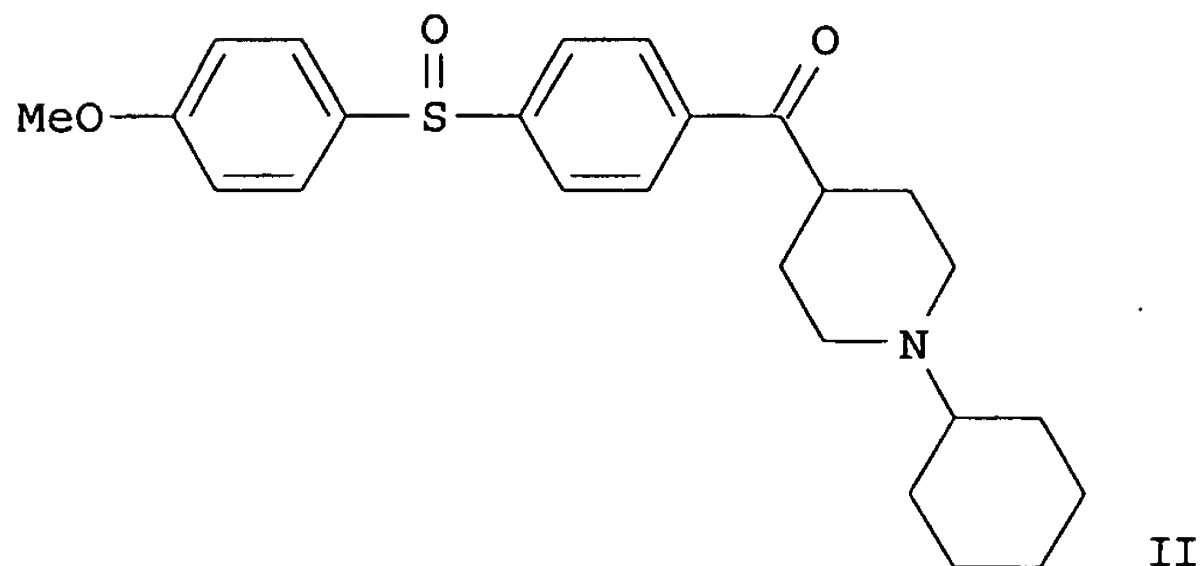
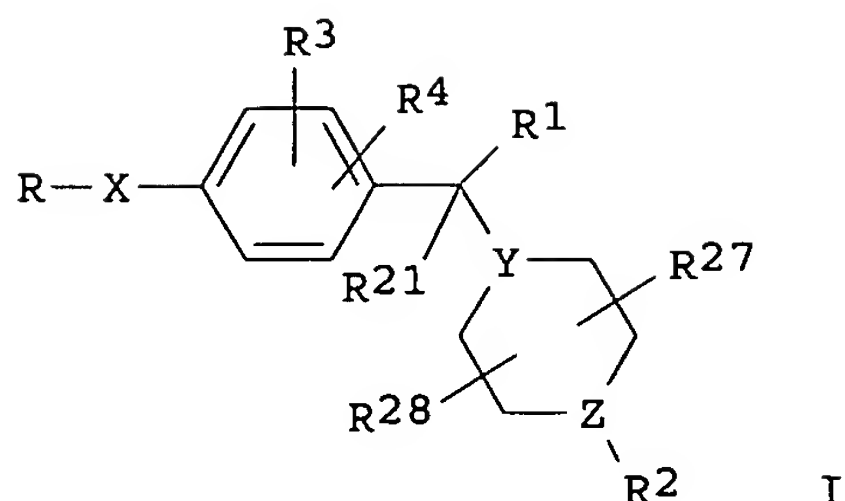
PRIORITY APPLN. INFO.:

US 1995-392697	B2	19950223
US 1995-457712	B2	19950602
US 1996-602403	A2	19960216
US 1996-700628	A3	19960808
US 1998-195742	A3	19981119
US 2000-482168	A3	20000112

OTHER SOURCE(S): MARPAT 130:252377

GI





AB Di-N-substituted piperazines or 1,4-di-substituted piperidines I [one of Y and Z is N and the other is N, CH, or C-alkyl; X = O, SOO-2, amino, substituted amino, CO, CH<sub>2</sub>, mono or disubstituted methylene, CS, CONR<sub>20</sub>, NR<sub>20</sub>SO<sub>2</sub>, NR<sub>20</sub>CO, SO<sub>2</sub>NR<sub>20</sub>, CH:CH, C.tplbond.C, NHC(O)NH; R = optionally substituted Ph, aryl, cycloalkyl; R<sub>1</sub>, R<sub>21</sub> = H, CN or optionally substituted alkyl; R<sub>2</sub> = optionally substituted cycloalkyl or piperidyl; R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>20</sub>, R<sub>27</sub>, R<sub>28</sub> are as defined in the specification], muscarinic antagonists, were prepared E.g., II was prepared

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:120328 HCAPLUS

DOCUMENT NUMBER: 130:296863

TITLE: Total Synthesis of (+)-Himbacine and (+)-Himbeline

AUTHOR(S): Chackalamannil, Samuel; Davies, Robert J.; Wang,

Yuguang; Asberom, Theodros; Doller, Dario;

Wong, Jesse; Leone, Daria; McPhail, Andrew T.

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Journal of Organic Chemistry (1999), 64(6), 1932-1940

CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 130:296863

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Himbacine (I) (R = Me), a complex piperidine alkaloid isolated from the bark of Australian magnolias, is a promising lead in Alzheimer's disease research due to its potent muscarinic receptor antagonist property. The authors have described a highly efficient synthetic strategy that resulted in the total synthesis of I in about 10% overall yield and isohimbacine (II), an unnatural isomer of himbacine, in 18% overall yield. The total synthesis of himbacine was initially approached using an intramol. Diels-Alder reaction as the key step to generate intermediate (III) followed by a [3 + 2] cycloaddn. with nitron (IV) to produce the isoxazolidine derivative (V). Methylation followed by catalytic reduction of V gave 12'-hydroxyhimbacine, which, upon dehydration, gave II as the sole product. In an alternative approach, an all-encompassing intramol. Diels-Alder reaction of an appropriately substituted tetraene derivative (VI), which bears the entire latent carbon framework and functional group substitution of himbacine, gave the desired advanced tricyclic intermediate, which was readily converted to (+)-himbeline (I) (R = H) (VII) and (+)-himbacine.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:65892 HCAPLUS

DOCUMENT NUMBER: 128:140691

TITLE: Preparation of 1,4-disubstituted piperidines as muscarinic antagonists

INVENTOR(S): Asberom, Theodros; Lowe, Derek B.; Green, Michael J.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9801425	A1	19980115	WO 1997-US11176	19970708
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2259655	AA	19980115	CA 1997-2259655	19970708
CA 2259655	C	20030513		
AU 9735810	A1	19980202	AU 1997-35810	19970708
AU 728592	B2	20010111		
EP 912515	A1	19990506	EP 1997-932321	19970708
EP 912515	B1	20021113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI, RO				
NZ 333513	A	20000428	NZ 1997-333513	19970708
JP 3068206	B2	20000724	JP 1998-505232	19970708
JP 11514671	T2	19991214		
AT 227708	E	20021115	AT 1997-932321	19970708
ES 2182104	T3	20030301	ES 1997-932321	19970708
PT 912515	T	20030331	PT 1997-932321	19970708
KR 2000023599	A	20000425	KR 1999-700045	19990107

PRIORITY APPLN. INFO.: US 1996-678618 A 19960710  
 WO 1997-US11176 W 19970708  
 OTHER SOURCE(S): MARPAT 128:140691  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; X = a bond, O, S, etc.; R = C3-6 cycloalkyl, II, III, etc.; R1 = H, CN, CF3, etc.; R2 = cycloalkyl, cycloalkenyl, t-butoxycarbonyl, (un)substituted 4-piperidinyl; R3, R4 = H, halo, CF3, etc.; R5, R6 = H, alkyl, CF3, etc.], useful for treating cognitive disorders such as Alzheimer's disease, were prepared. Compds. I are capable of enhancing acetylcholine (ACh) release with an ACh'ase inhibitors. Thus, a 5-step detailed synthesis of the title compound IV is described. The title compound V showed Ki of 40.8 nM against m2 receptor binding and of 66.4 nM against m4 receptor binding.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

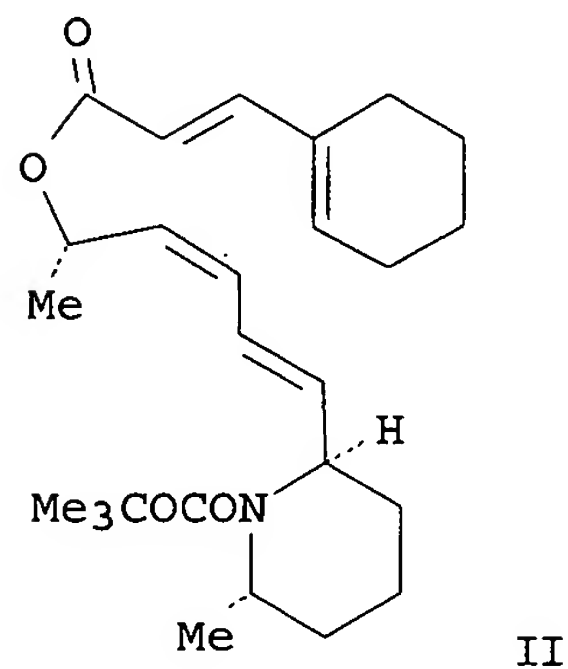
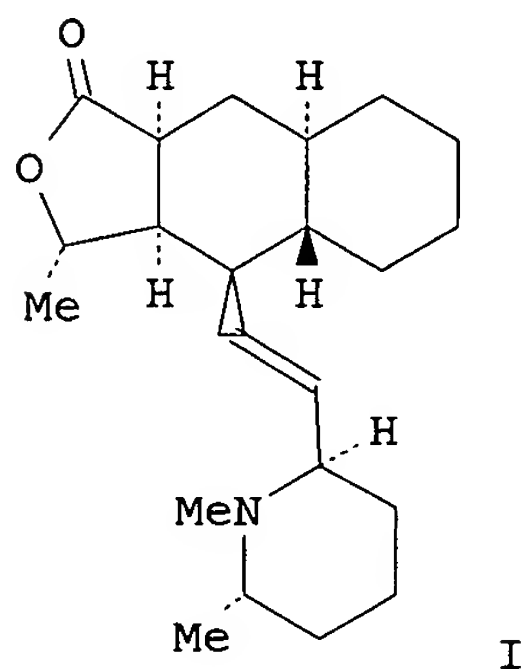
ACCESSION NUMBER: 1997:162000 HCAPLUS  
 TITLE: Synthesis and biological evaluation of himbacine and analogs.  
 AUTHOR(S): Chackalamannil, Samuel; Davies, Robert J.; Doller, Dario; Wang, Yuguang; Asberom, Theodros; Leone, Daria; McQuade, Robert; Ruperto, Vilma; McPhail, Andrew T.  
 CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA  
 SOURCE: Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), MEDI-167. American Chemical Society: Washington, D. C.  
 CODEN: 64AOAA  
 DOCUMENT TYPE: Conference; Meeting Abstract  
 LANGUAGE: English

AB Himbacine (1) is a tetracyclic piperidine alkaloid isolated from the bark of the Australian pine tree of Galbulimima species. It has attracted considerable attention due to its promising biol. property as a selective muscarinic receptor antagonist. Enhancement of synaptic acetylcholine levels by selective inhibition of presynaptic muscarinic receptors is a promising therapeutic approach for the treatment of senile dementia associated with Alzheimer's disease. Himbacine is a potent inhibitor of the muscarinic receptor of M2 subtype with 10 to 20-fold selectivity toward other receptors. In the context of our efforts to develop potent and selective muscarinic receptor antagonists, we have developed a general and practical approach for the synthesis of himbacine analogs. We wish to report the syntheses of (+)-himbacine (1) and a number of its analogs using a highly convergent and practical approach. Addnl., a systematic evaluation of the structure-activity relationship and selectivity of these compds. against various muscarinic receptors will be presented.

L35 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:616758 HCAPLUS  
 DOCUMENT NUMBER: 126:8335  
 TITLE: A Highly Efficient Total Synthesis of (+)-Himbacine  
 AUTHOR(S): Chackalamannil, Samuel; Davies, Robert J.; Asberom, Theodros; Doller, Dario; Leone, Daria

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA  
 SOURCE: Journal of the American Chemical Society (1996), 118(40), 9812-9813  
 CODEN: JACSAT; ISSN: 0002-7863  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 126:8335  
 GI



AB Himbacine (I) is a complex tetracyclic alkaloid isolated from the Australian pine tree of *Galbulimima* species. It is a potent muscarinic antagonist and, therefore, a promising therapeutic lead in the discovery of treatment for Alzheimer's disease. (+)-I has been synthesized in eleven linear steps from (S)-2-methylpiperidine.L-tartrate salt in 9.7% yield. The key step involves an all-encompassing, enantioselective intramol. Diels-Alder reaction of tetraene derivative II which bears the entire latent carbon framework and functional group substitution of I.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

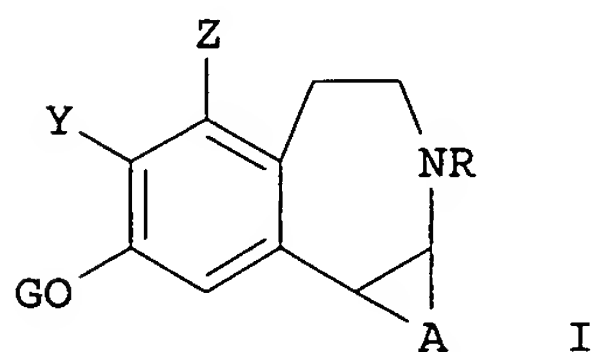
ACCESSION NUMBER: 1996:414670 HCAPLUS  
 TITLE: Himbacine analogs as muscarinic receptor antagonists  
 AUTHOR(S): Doller, Dario; Chackalamannil, Samuel; **Asberom, Theodros**; Leone, Daria  
 CORPORATE SOURCE: Chemistry Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA  
 SOURCE: Book of Abstracts, 212th ACS National Meeting, Orlando, FL, August 25-29 (1996), MEDI-082. American Chemical Society: Washington, D. C.  
 CODEN: 63BFAF  
 DOCUMENT TYPE: Conference; Meeting Abstract  
 LANGUAGE: English

AB Himbacine, an alkaloid isolated from barks of trees of *Galbulimima* species, has long been recognized as a potential lead for the development of selective muscarinic receptor antagonists in Alzheimer disease studies. Despite its complex structure, remarkably its eight chiral centers, we have developed synthetic methods that allowed us to study the structure-activity relationship of himbacine analogs, all of which display the alkaloid's original tricycle moiety. We have examined the importance of the double bond, as well as other substituents, in the bridge region.

Also, substitution on the lactone ring and the nature of the basic unit were studied. As a result, we have demonstrated the crucial nature of the trans-6'-Me group in determining potencies and selectivities against muscarinic receptors. Modeling and exptl. results point towards the existence of key hydrophobic interactions between himbacine and the receptor near the basic site.

L35 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1995:255608 HCAPLUS  
 DOCUMENT NUMBER: 123:83224  
 TITLE: 4,5-bridged-2,3,4,5-tetrahydro-1H-3-benzazepine-7-ols and derivatives and compositions and methods employing such compounds for the treatment of psychoses???, drug dependence, D1 dependent neurol. disorder or pain  
 INVENTOR(S): Asberom, Theodros; O'Connor, Edward; Berger, Joel G.; Clader, John W.  
 PATENT ASSIGNEE(S): Schering Corp., USA  
 SOURCE: U.S., 25 pp. Cont.-in-part of U.S. Ser. No. 474,428, abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5362728	A	19941108	US 1992-915710	19920729
WO 9111437	A1	19910808	WO 1991-US503	19910131
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1990-474428	B2 19900202
			WO 1991-US503	W 19910131
OTHER SOURCE(S):		MARPAT 123:83224		
GI				



AB Novel benzazepines of the formula I or a pharmaceutically acceptable salt thereof, wherein R represents H, alkyl, allyl or cyclopropylmethyl; A represents [CR<sub>1</sub>R<sub>2</sub>]<sub>n</sub>; n represents 3 or 4; R<sub>1</sub> and R<sub>2</sub> may be the same or different and each independently represents H, OH, alkyl, alkoxy, Ph or substituted Ph, with the proviso that R<sub>1</sub> and R<sub>2</sub> on the same carbon atom are not both OH, or R<sub>1</sub> and R<sub>2</sub> on the same carbon atom together represent :O; G represents H, R<sub>3</sub>(CO) or ArNHCO; R<sub>3</sub> represents H, alkyl, alkoxy, Ph or substituted phenyl; Ar represents Ph or substituted phenyl; and Y and Z may be the same or different and each is independently selected from H, halo, alkyl, alkoxy or haloalkyl; the pharmaceutically acceptable salts thereof, and pharmaceutical compns. thereof, useful in the treatment of

psychoses, drug dependence, D1 dependent neurol. disorder or pain are disclosed. Conditioned avoidance response test (min. ED mpk p.o.) in squirrel monkey: from 3 to >10; inhibition consts. Ki (nM) for D-1 receptor binding: from 2.8 to 335, compared to from 380 to >10,000 for the D-2 site. Pharmaceutical formulations were given.

L35 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:511485 HCAPLUS

DOCUMENT NUMBER: 117:111485

TITLE: Preparation of 4,5-cycloalkano-3-benzazepin-7-ols as dopaminergic D1 antagonists

INVENTOR(S): Asberom, Theodros; O'Connor, Edward; Berger, Joel Gilbert; Clader, John Welch

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

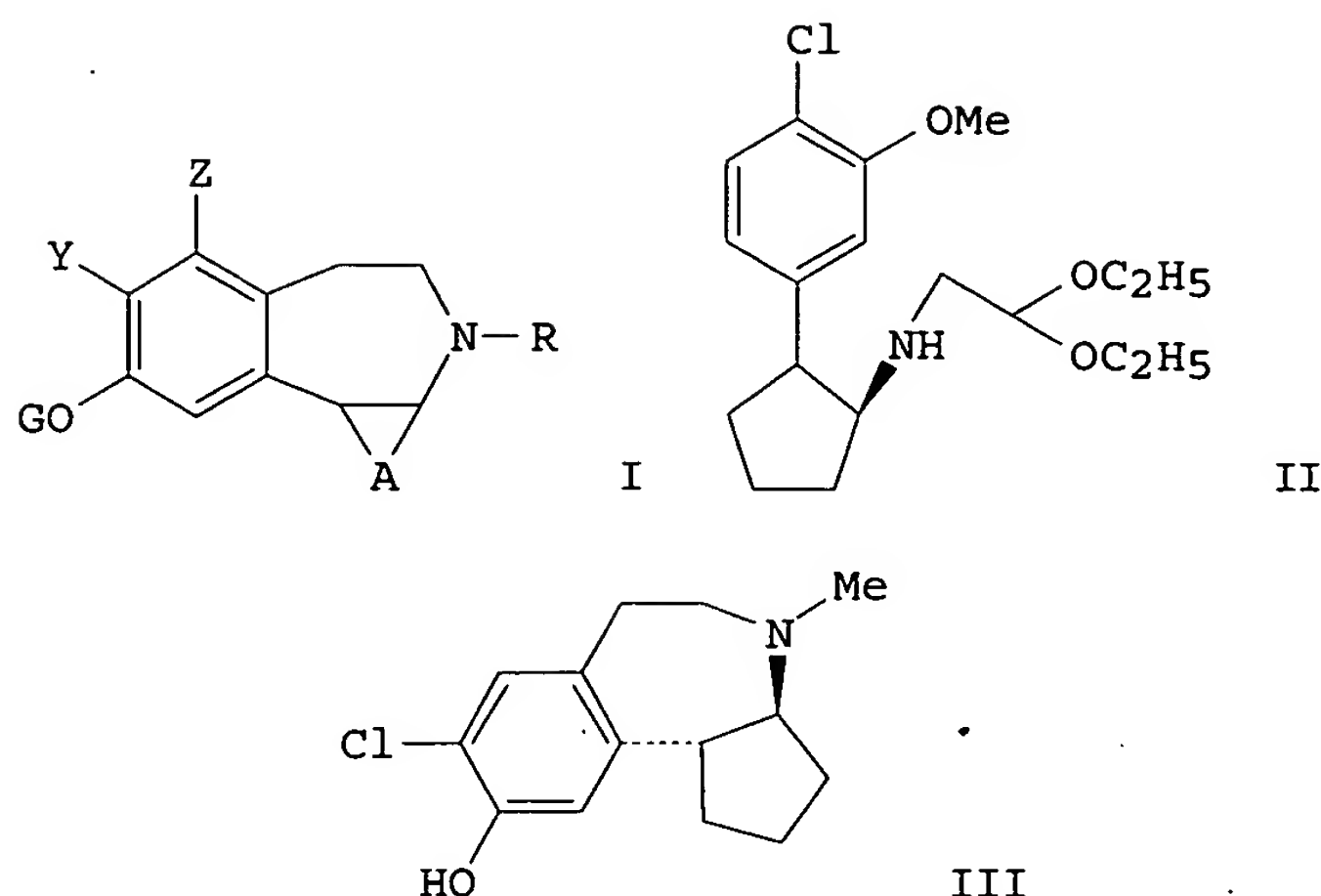
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9111437	A1	19910808	WO 1991-US503	19910131
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2075181	AA	19910803	CA 1991-2075181	19910131
CA 2075181	C	19971209		
EP 513174	A1	19921119	EP 1991-904114	19910131
EP 513174	B1	19950816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05504769	T2	19930722	JP 1991-504442	19910131
JP 06013474	B4	19940223		
AU 646432	B2	19940224	AU 1991-72432	19910131
ES 2075429	T3	19951001	ES 1991-904114	19910131
US 5362728	A	19941108	US 1992-915710	19920729
FI 9203458	A	19920731	FI 1992-3458	19920731
NO 9203042	A	19921001	NO 1992-3042	19920731
PRIORITY APPLN. INFO.:			US 1990-474428	A 19900202
			WO 1991-US503	W 19910131

OTHER SOURCE(S): MARPAT 117:111485

GI





AB Title compds. I [R = H, alkyl, allyl, cyclopropylmethyl; A = (CR<sub>1</sub>R<sub>2</sub>)<sub>n</sub>; n = 3, 4; R<sub>1</sub>, R<sub>2</sub> = H, OH, alkyl, alkoxy, (substituted) Ph; R<sub>1</sub> and R<sub>2</sub> on the same C atom both ≠ OH, or R<sub>1</sub> and R<sub>2</sub> on same C = O; G = H, R<sub>3</sub>CO, ArNHCO; R<sub>3</sub> = H, alkyl, alkoxy, (substituted) Ph; Ar = (substituted) Ph; Y, Z = H, halo, alkyl, alkoxy, haloalkyl] were prepared as dopaminergic D<sub>1</sub> antagonists useful as antipsychotics, analgesics, and for the treatment of drug dependence. Thus, alkylated amine II (preparation given) was cyclized in the presence of MeSO<sub>3</sub>H to give the cyclic enamine, which was reduced by NaCNBH<sub>3</sub> to give I [Y = Cl; G = Me; A = (CH<sub>2</sub>)<sub>3</sub>; Z = H; R = H]. N-ethoxycarbonylation of the latter by ClCO<sub>2</sub>Et, followed by LiAlH<sub>4</sub> reduction and ether cleavage by BBr<sub>3</sub> gave title compound III. III had K<sub>i</sub> of 2.8 nM against binding of 3H-Sch 23390 at dopaminergic D<sub>1</sub> receptors. Formulations containing I were prepared

L35 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:20961 HCAPLUS

DOCUMENT NUMBER: 116:20961

TITLE: Preparation of 4,5-cycloalkano-3-benzazepin-7-ols as nervous system agents.

INVENTOR(S): Asberom, Theodoros; O'Connor, Edward; Berger, Joel Gilbert; Clader, John Welch

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

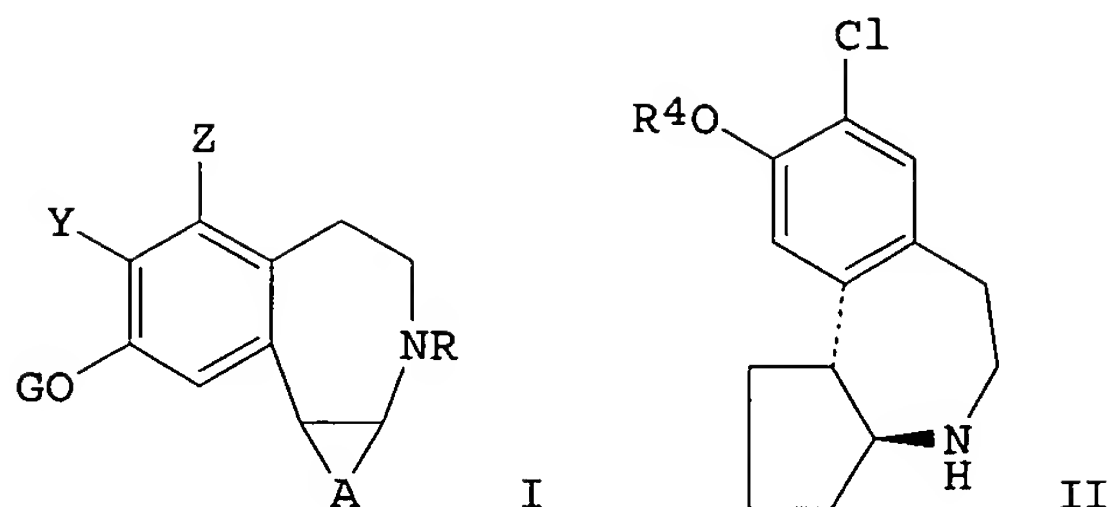
DOCUMENT TYPE: Patent

LANGUAGE: English

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9111437 A1		19910808	WO 1991-US503	19910131
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1990-464428	19900202
			US 1990-474428	19900202
OTHER SOURCE(S):		MARPAT 116:20961		

GI



AB Title compds. [I; R = H, alkyl, allyl, cyclopropylmethyl; A = (CR<sub>1</sub>R<sub>2</sub>)<sub>n</sub>, R<sub>1</sub>, R<sub>2</sub> = H, HO, alkyl, alkoxy, (substituted) Ph, R<sub>1</sub>, R<sub>2</sub> on the same C ≠ HO, R<sub>1</sub>, R<sub>2</sub> on the same C = O; G = H, ArNHCO, Ar = (substituted) Ph, R<sub>3</sub>CO, R<sub>3</sub> = H, alkyl, alkoxy, (substituted) Ph; Y, Z = H, halo, alkyl, alkoxy, haloalkyl; n = 3,4] useful for treating psychoses, drug dependence, D1 dependent neurol. disorder or pain, are prepared Benzoxazine II (R<sub>4</sub> = Me) (preparation from cyclopentanone and 5-bromo-2-chloroanisole given), in CH<sub>2</sub>Cl<sub>2</sub> at -78° was treated with BBr<sub>3</sub>; the reaction mixture was stirred at -78° for 1 h, then at room temperature for 2 h to give II [R<sub>4</sub> = H]. I showed biol. activity (e.g., suppression of conditioned avoidance in squirrel monkeys) for treating the mentioned disorders. Capsule and tablet formulations are given.

L35 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:535752 HCAPLUS

DOCUMENT NUMBER: 115:135752

TITLE: The chemistry of cyclic vinyl ethers. 6. Total synthesis of polyether ionophore antibiotics of the calcimycin (A-23187) class

AUTHOR(S): Boeckman, Robert K., Jr.; Charette, Andre B.; Asberom, Theodros; Johnston, Brian H.

CORPORATE SOURCE: Dep. Chem., Univ. Rochester, Rochester, NY, 14627, USA  
SOURCE: Journal of the American Chemical Society (1991), 113(14), 5337-53

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 115:135752

GI

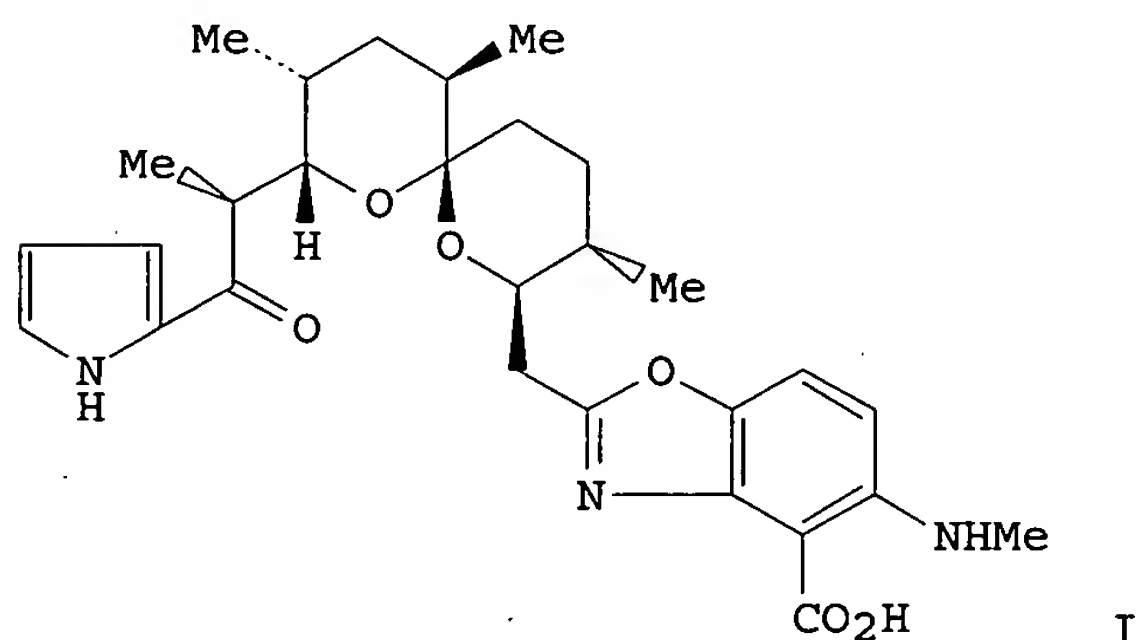
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB An extremely convergent (longest linear sequence 16 steps), stereoselective, and potentially general synthesis of the antibiotic ionophores was devised. The key steps involve a coupling reaction between the chiral nonracemic subunits dihydropyran I (as the α-lithio anion) and bromide II. Subsequent acid-promoted cyclization directly produces the spirocyclic ring system found in the ionophore X-14885A (III; R = H, R<sub>1</sub> = OH). Alternatively, cyclopropanation of substituted vinyl



ether IV followed by acid treatment afforded the spiroketal V that was subsequently converted into the polyether ionophore calcimycin (III; R = Me, R1 = NHMe) and also Cezomycin (III; R = Me, R1 = H).

L35 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1988:5753 HCAPLUS  
 DOCUMENT NUMBER: 108:5753.  
 TITLE: A convergent general synthetic protocol for construction of spirocyclic ketal ionophores: an application to the total synthesis of (-)-A-23187 (calcimycin)  
 AUTHOR(S): Boeckman, Robert K., Jr.; Charette, Andre B.; Asberom, Theodros; Johnston, Brian H.  
 CORPORATE SOURCE: Dep. Chem., Univ. Rochester, Rochester, NY, 14627, USA  
 SOURCE: Journal of the American Chemical Society (1987), 109(24), 7553-5  
 CODEN: JACSAT; ISSN: 0002-7863  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 108:5753  
 GI



AB A flexible and efficient synthetic strategy for the synthesis of calcimycin (I) is detailed. Coupling of the anion derived from a suitably substituted dihydropyran with an appropriately substituted bromide followed by cyclopropanation and cyclization of the resulting cyclopropyl ethers provides a key, differentially protected, spiroketal which was elaborated to I. Overall, the route is highly convergent and efficient (13 steps along the longest sequence), and readily lends itself to the preparation of related ionophores and analogs thereof.

L35 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1986:533632 HCAPLUS  
 DOCUMENT NUMBER: 105:133632  
 TITLE: Application of cyclic vinyl ether carbanions: progress towards enantioselective synthesis of calcimycin  
 AUTHOR(S): Asberom, Theodros  
 CORPORATE SOURCE: Univ. Rochester, Rochester, NY, USA  
 SOURCE: (1985) 244 pp. Avail.: Univ. Microfilms Int., Order No. DA8516459  
 From: Diss. Abstr. Int. B 1986, 46(6), 1918  
 DOCUMENT TYPE: Dissertation  
 LANGUAGE: English

AB Unavailable

=&gt; =&gt; d stat que nos

L4 STR  
 L10 STR  
 L12 25437 SEA FILE=REGISTRY SSS FUL L4 AND L10  
 L13 STR  
 L15 5 SEA FILE=REGISTRY SUB=L12 SSS FUL L13  
 L16 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15  
 L17 25432 SEA FILE=REGISTRY ABB=ON PLU=ON L12 NOT L15  
 L18 183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE  
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 OR L22 OR L32)  
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 L36 85 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOBBS D"/AU OR "HOBBS D  
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L37 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:981365 HCAPLUS

DOCUMENT NUMBER: 141:379943

TITLE: Preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.;  
 Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Mallams,  
 Alan; Alvarez, Carmen S.; Keertikar, Kartik M.;  
 Rivera, Jocelyn; Chan, Tin-Yau; Madison, Vincent;  
 Fischmann, Thierry O.; Dillard, Lawrence W.; Tran,  
 Vinh D.; He, Zhen Min; James, Ray Anthony; Park,  
 Haengsoon; Paradkar, Vidyadhar M.; **Hobbs, Douglas  
 Walsh**

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacoepia, Inc.

SOURCE: U.S. Pat. Appl. Publ., 1044 pp., Cont.-in-part of U.S.  
 Ser. No. 654,546.

CODEN: USXXCO

DOCUMENT TYPE: Patent

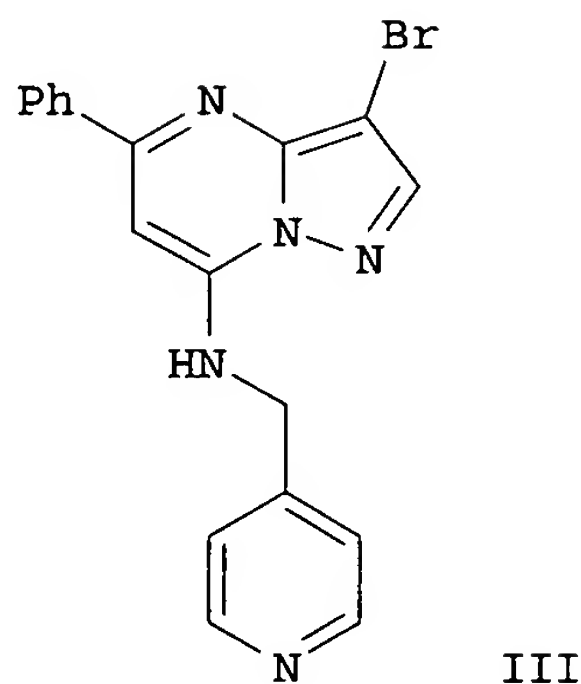
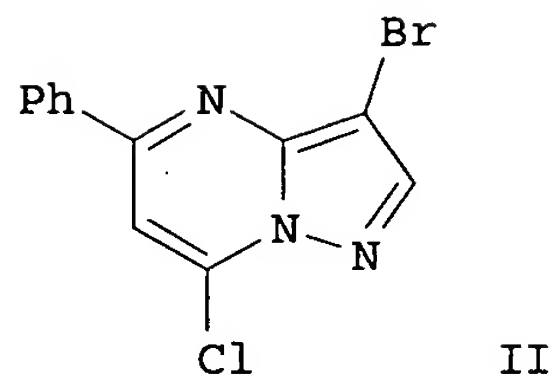
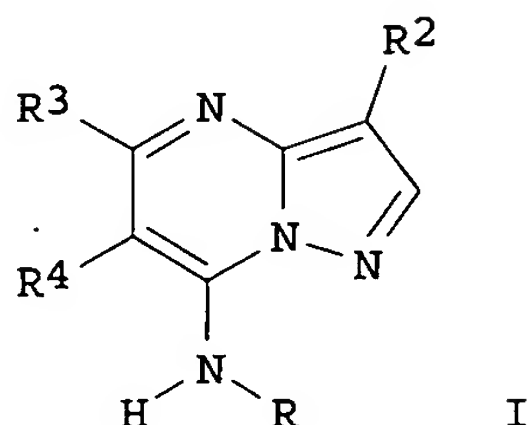
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004209878	A1	20041021	US 2004-776988	20040211
US 2004209878	A1	20041021	US 2004-776988	20040211
PRIORITY APPLN. INFO.:			US 2002-408027P.	P 20020904
			US 2002-421959P	P 20021029
			US 2003-654546	A2 20030903
			US 2004-776988	A 20040211

GI



AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with 4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020  $\mu$ M and 0.029  $\mu$ M against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a

Part

III of I-III series.

IT 677278-60-3P 677278-83-0P 677278-88-5P  
 677281-50-4P 677281-71-9P 677281-76-4P  
 677285-84-6P 677286-62-3P 677287-60-4P  
 677289-03-1P

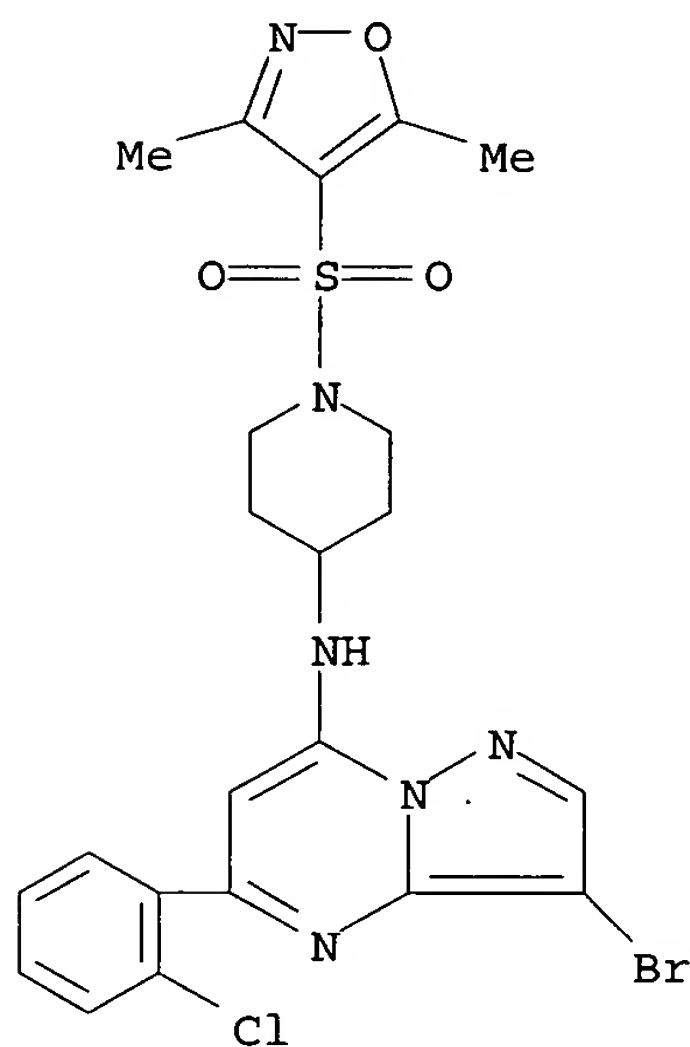
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors

for treating cancer)

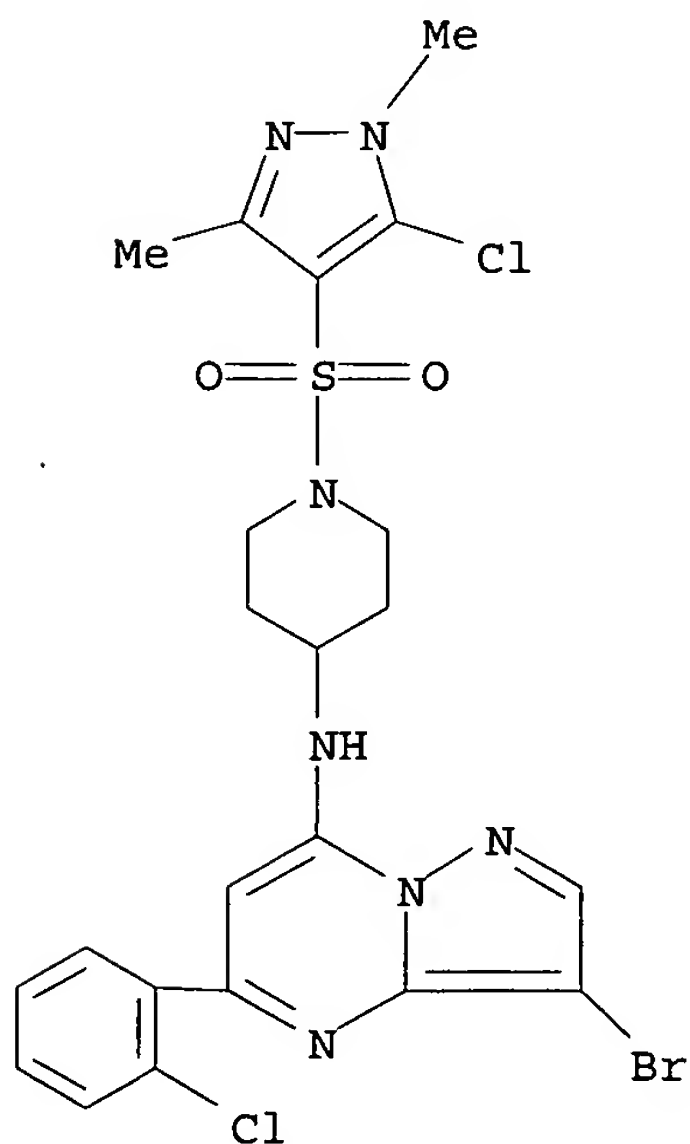
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CN 4-Piperidinamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677278-83-0 HCAPLUS

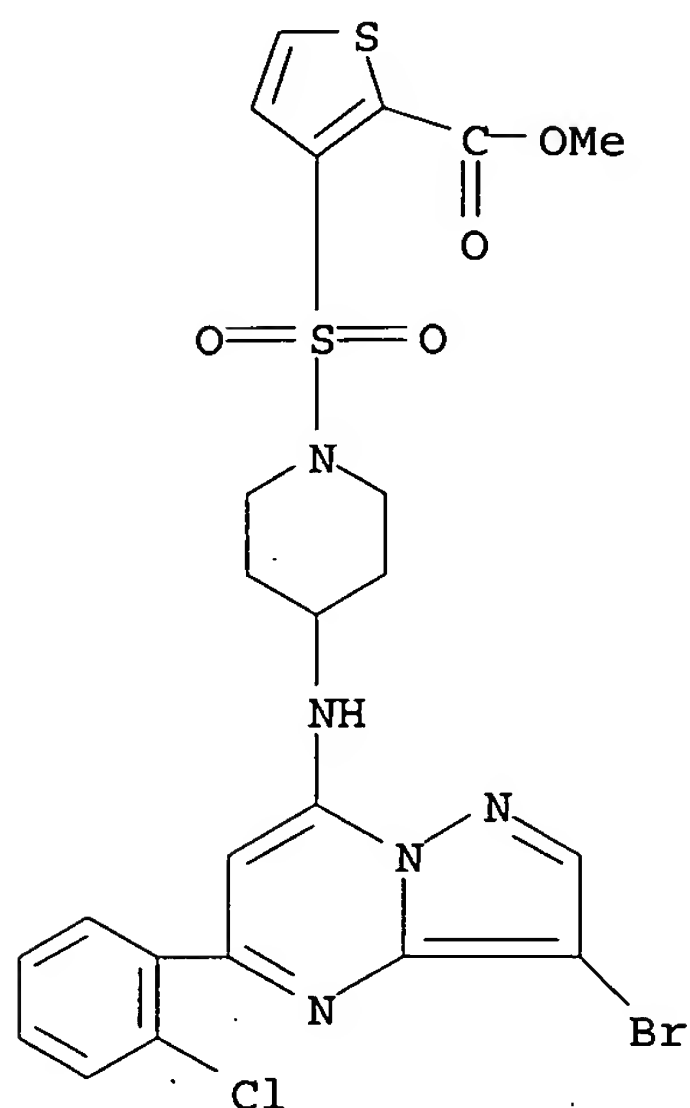
CN 4-Piperidinamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677278-88-5 HCAPLUS

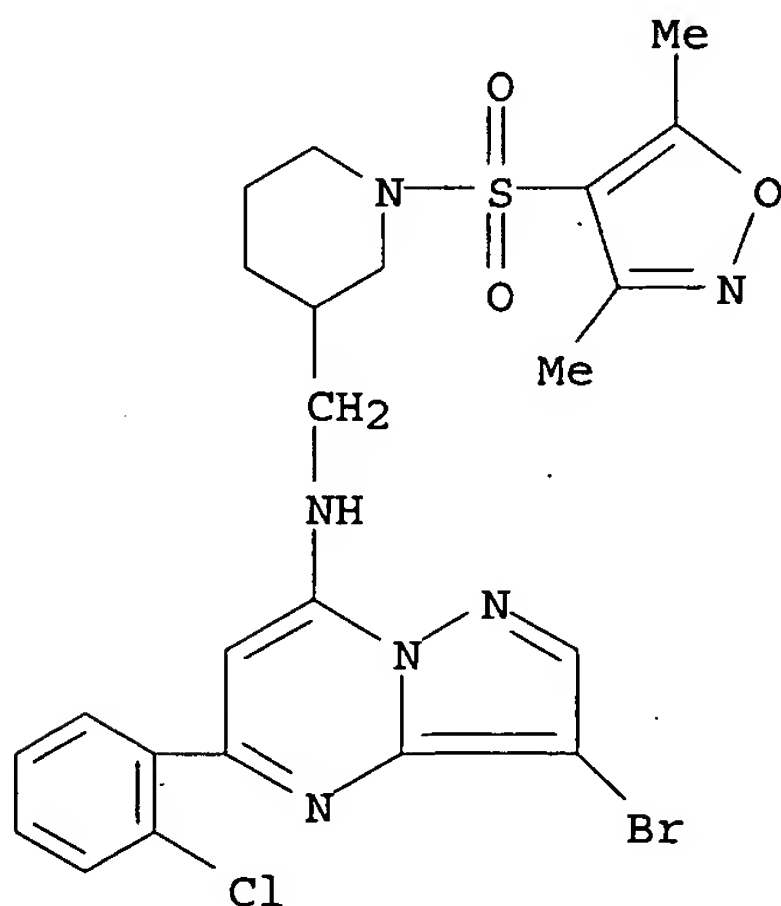
CN 2-Thiophenecarboxylic acid, 3-[[4-[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-

alpyrimidin-7-yl]amino]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



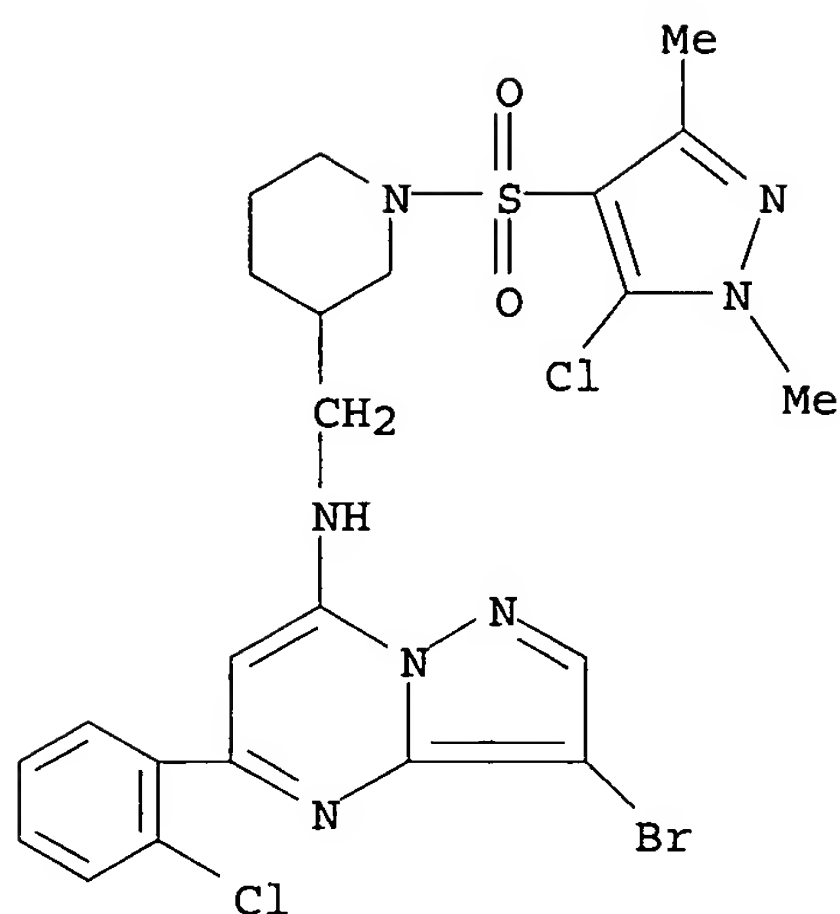
RN 677281-50-4 HCAPLUS

CN 3-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)



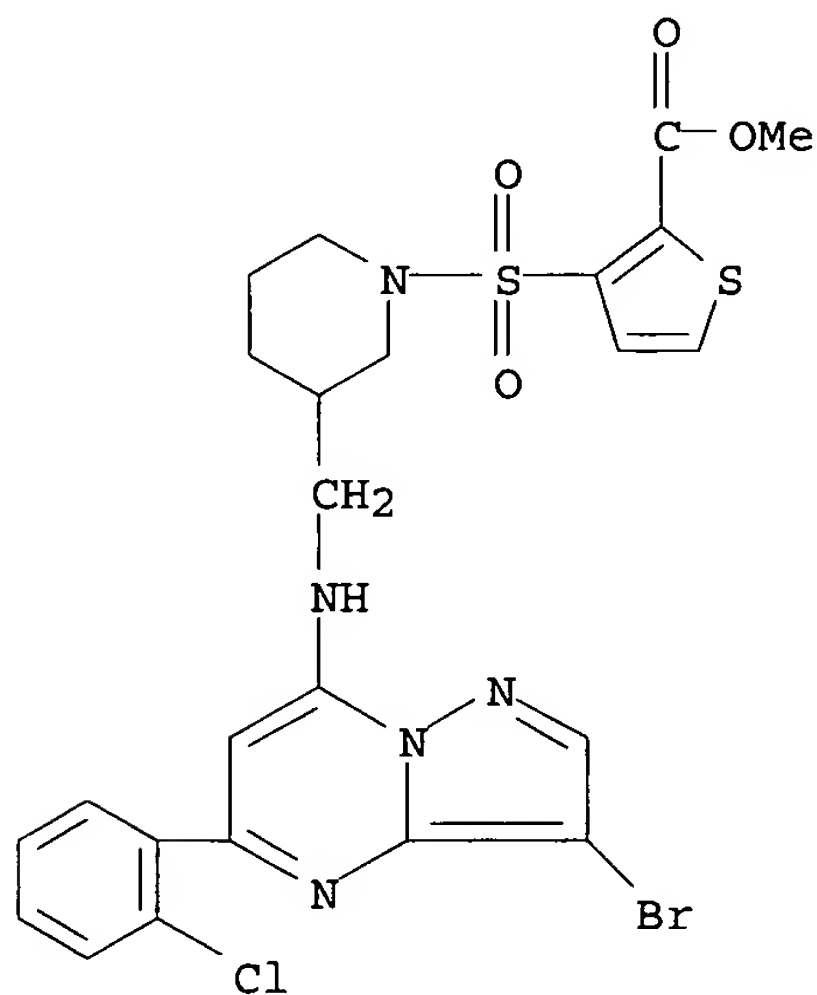
RN 677281-71-9 HCAPLUS

CN 3-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)



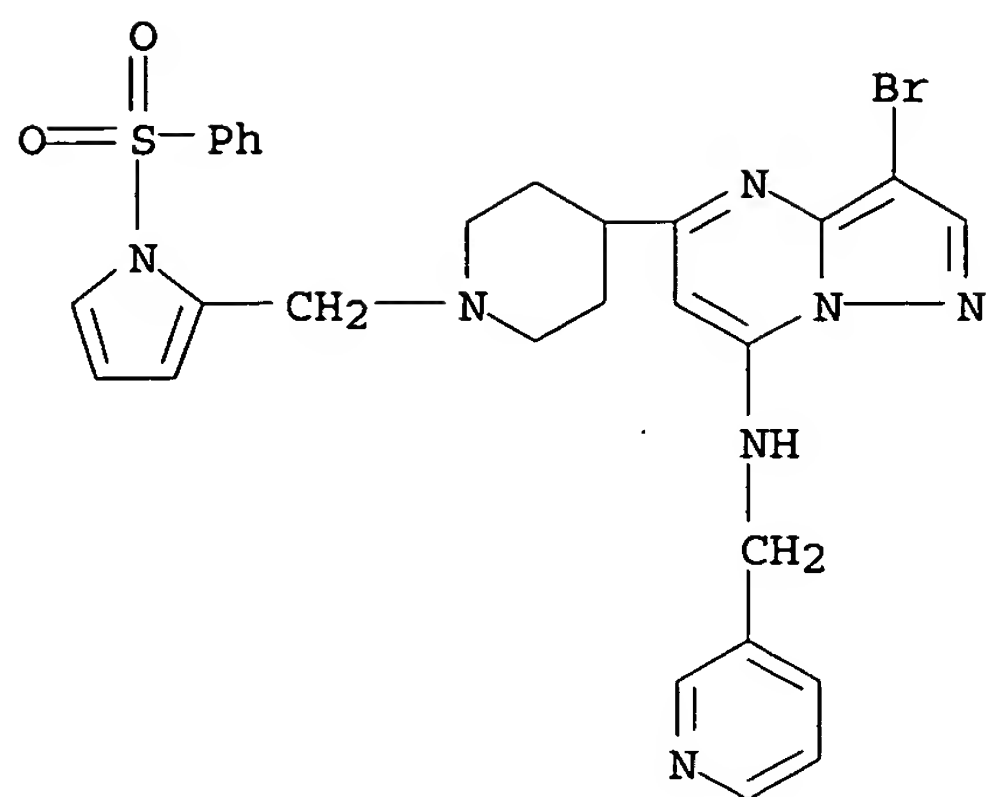
RN 677281-76-4 HCAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[[3-[[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]methyl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



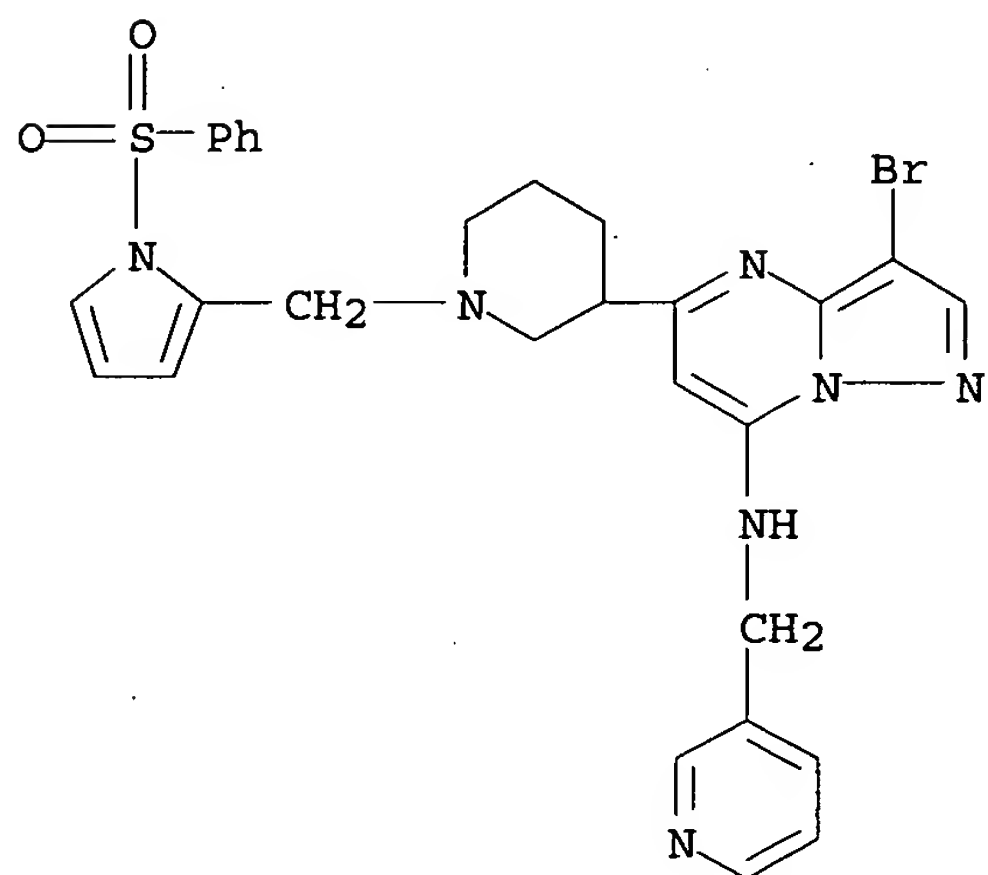
RN 677285-84-6 HCAPLUS

CN 1H-Pyrrole, 2-[[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



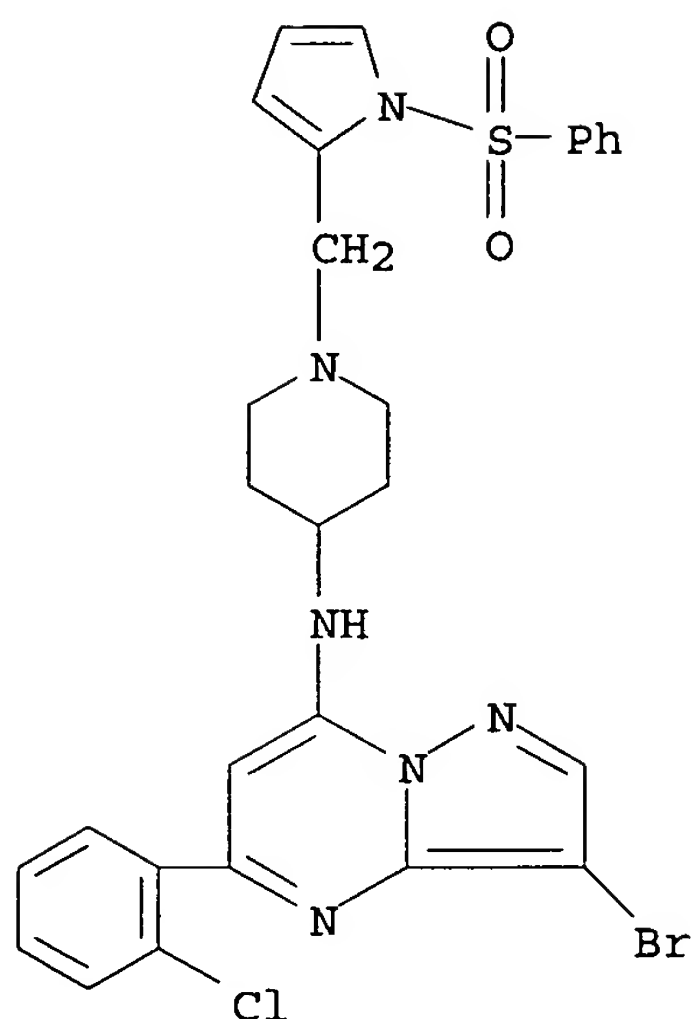
RN 677286-62-3 HCAPLUS

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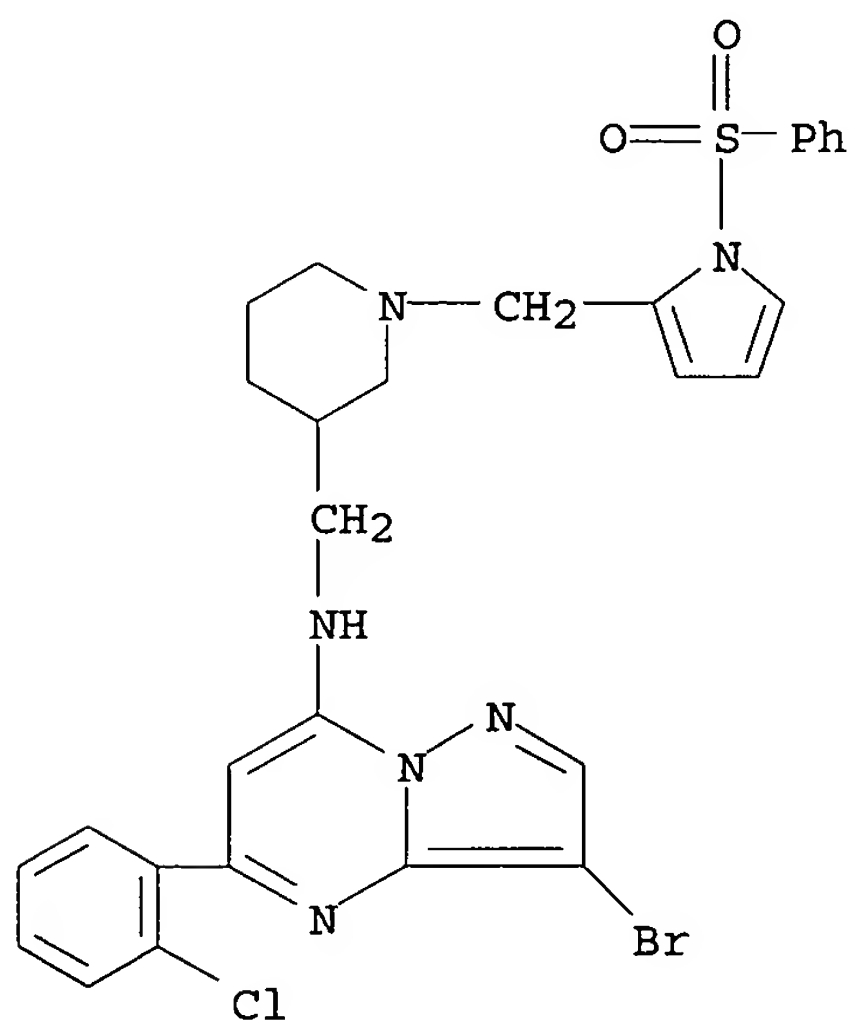


RN 677287-60-4 HCAPLUS

CN 1H-Pyrrole, 2-[[4-[[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]amino]-1-piperidinyl]methyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 677289-03-1 HCAPLUS  
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L37 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:980998 HCAPLUS  
 DOCUMENT NUMBER: 141:379942  
 TITLE: Preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors  
 INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Mallams, Alan; Alvarez, Carmen S.; Keertikar, Kartik M.;

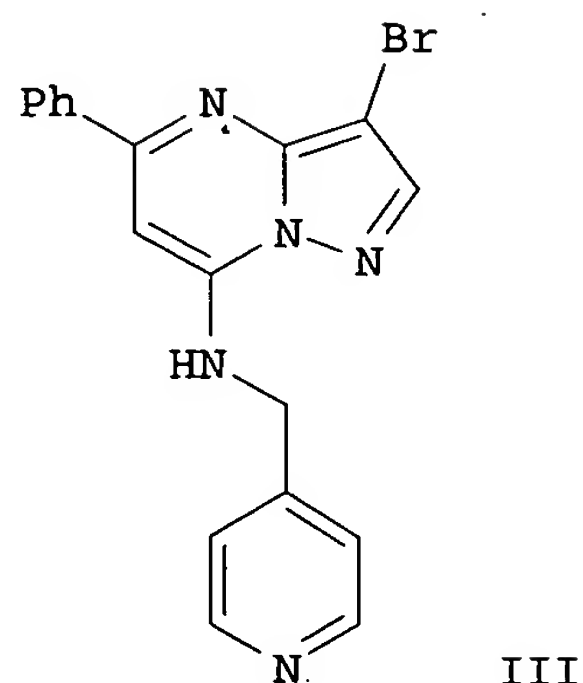
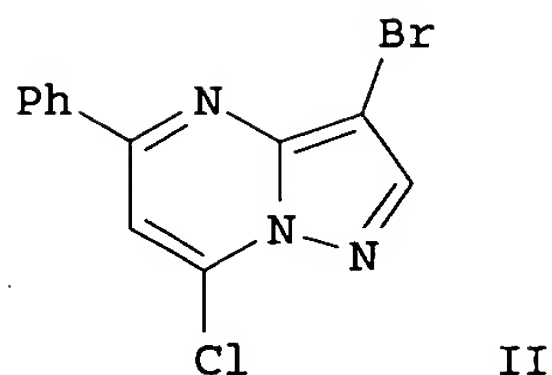
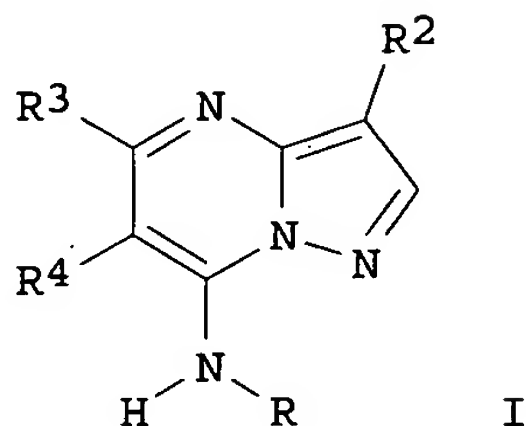


Rivera, Jocelyn; Chan, Tin-Yau; Madison, Vincent;  
Fischmann, Thierry O.; Dillard, Lawrence W.; Tran,  
Vinh D.; He, Zhen Min; James, Ray Anthony; Park,  
Haengsoon; Paradkar, Vidyadhar M.; **Hobbs, Douglas  
Walsh**

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia, Inc.  
SOURCE: U.S. Pat. Appl. Publ., 1044 pp., Cont.-in-part of U.S.  
Ser. No. 654,546.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004209878	A1	20041021	US 2004-776988	20040211
US 2004209878	A1	20041021	US 2004-776988	20040211
PRIORITY APPLN. INFO.:			US 2002-408027P	P 20020904
			US 2002-421959P	P 20021029
			US 2003-654546	A2 20030903
			US 2004-776988	A 20040211

GI



AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with

4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020  $\mu$ M and 0.029  $\mu$ M against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a

Part

II of I-III series.

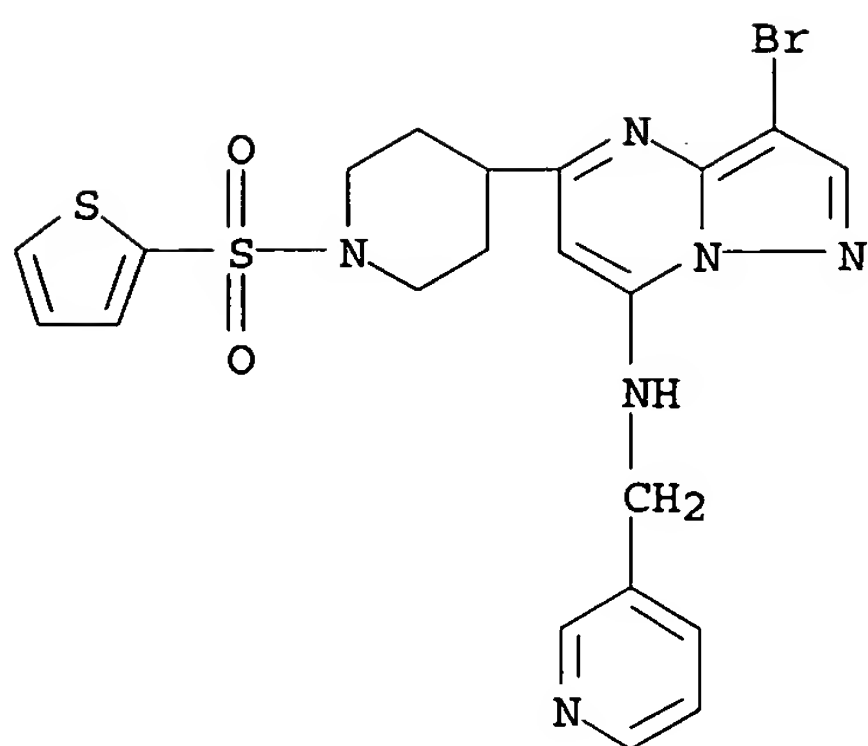
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RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors)

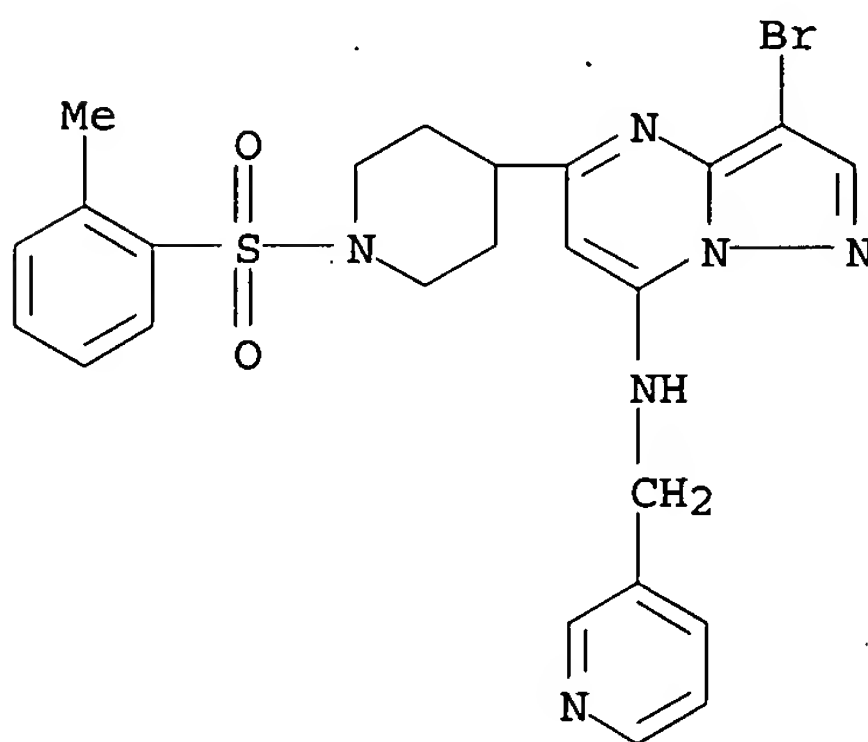
RN 677793-40-7 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)



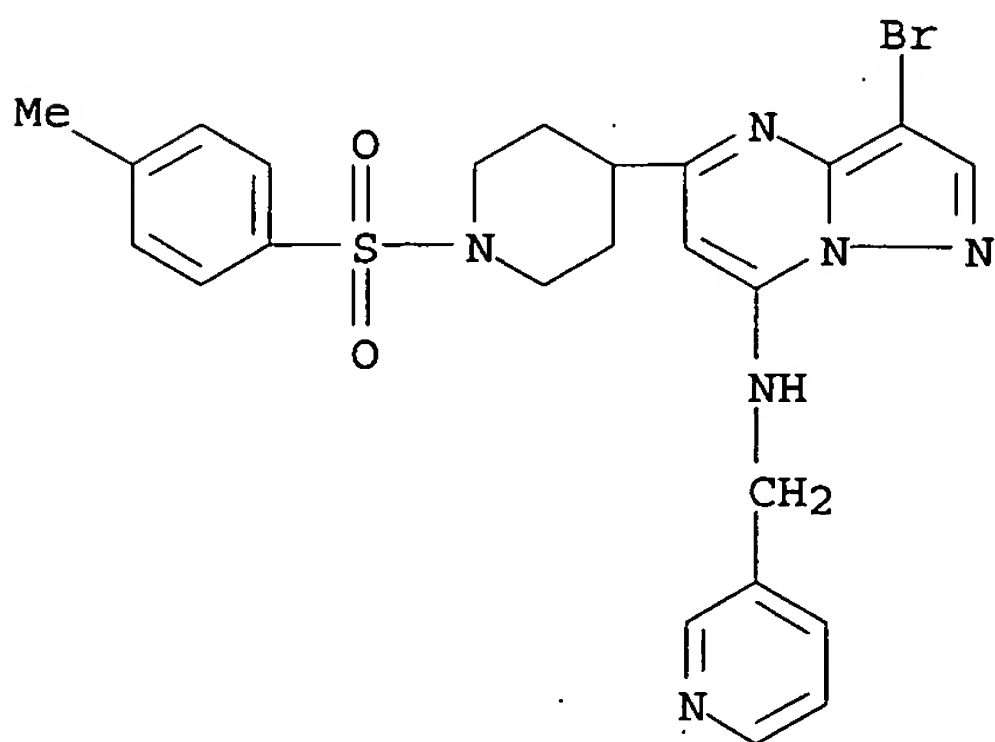
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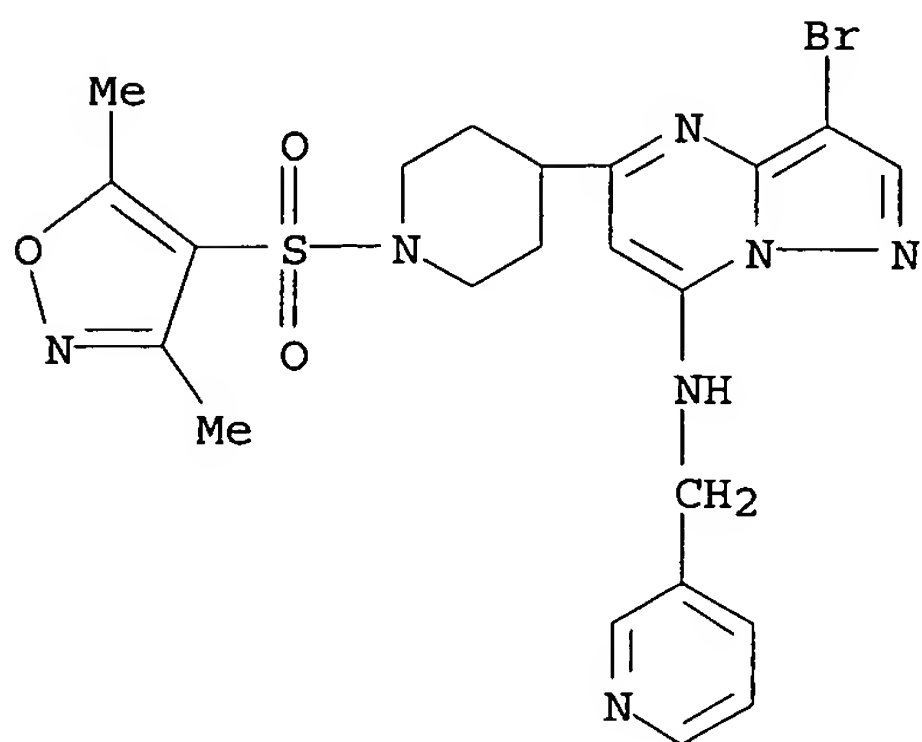
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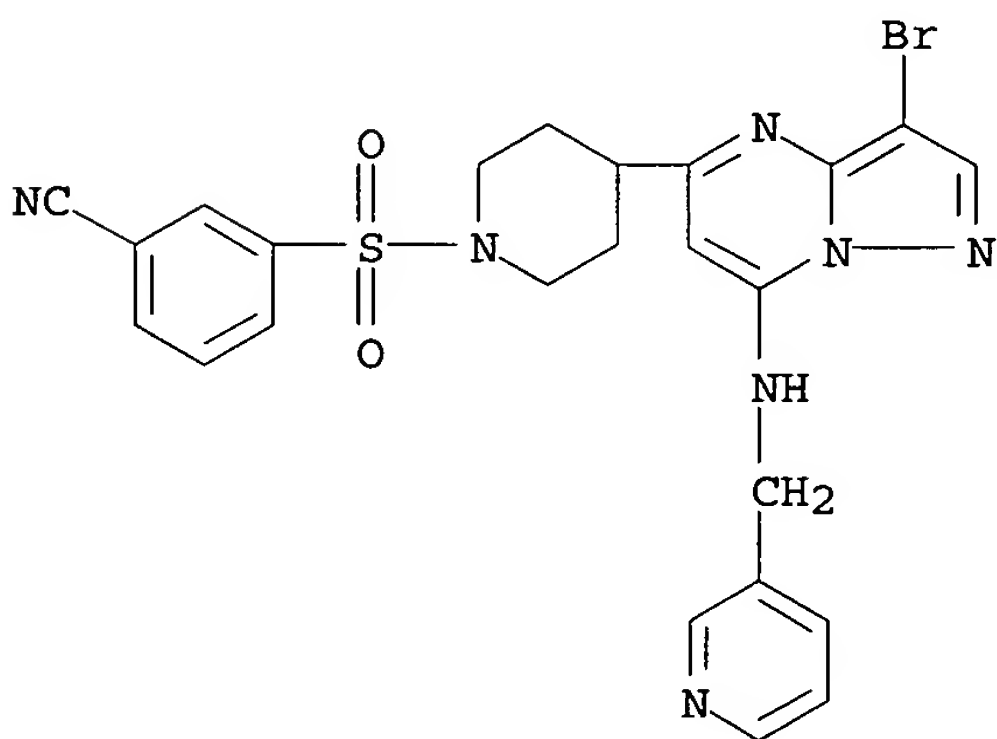
RN 677793-43-0 HCAPLUS

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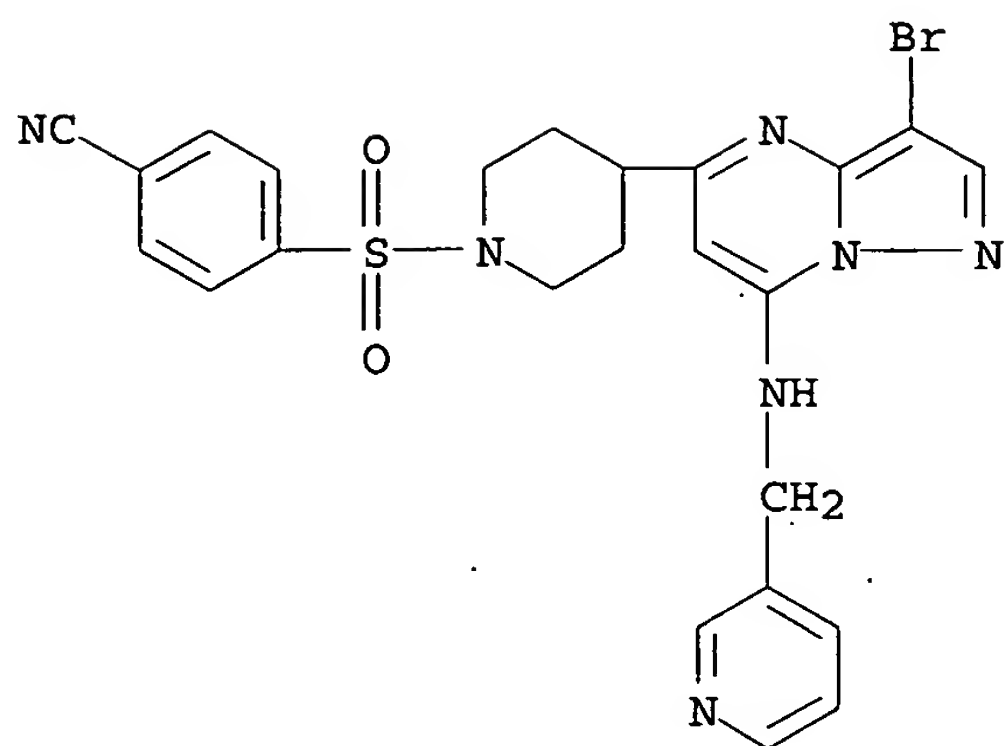
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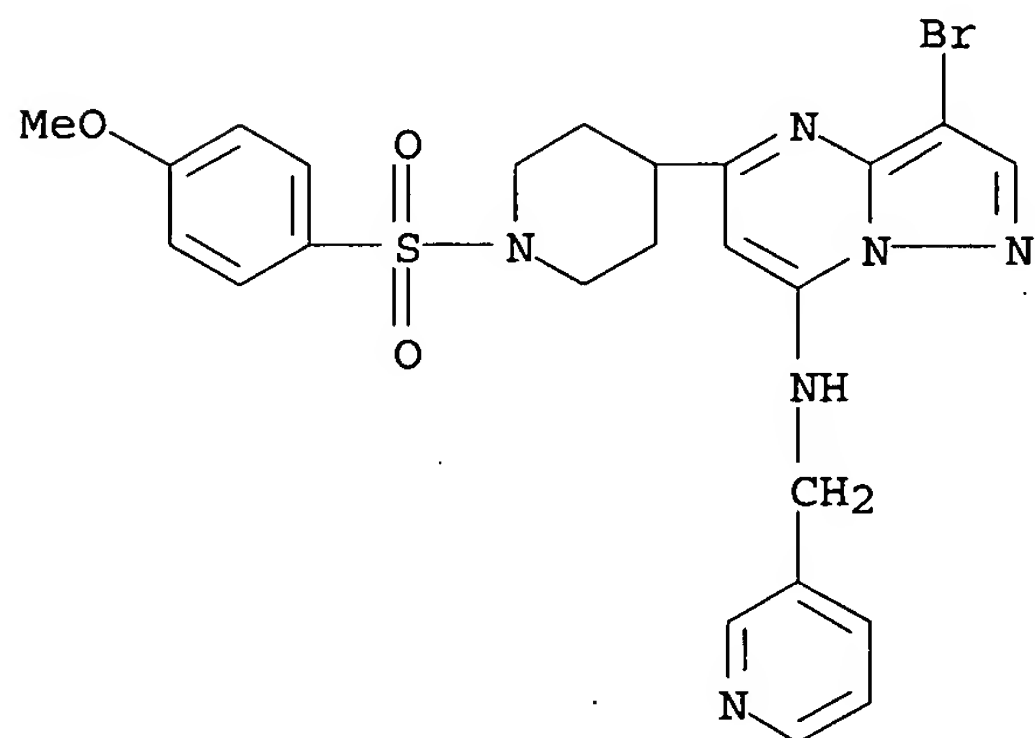


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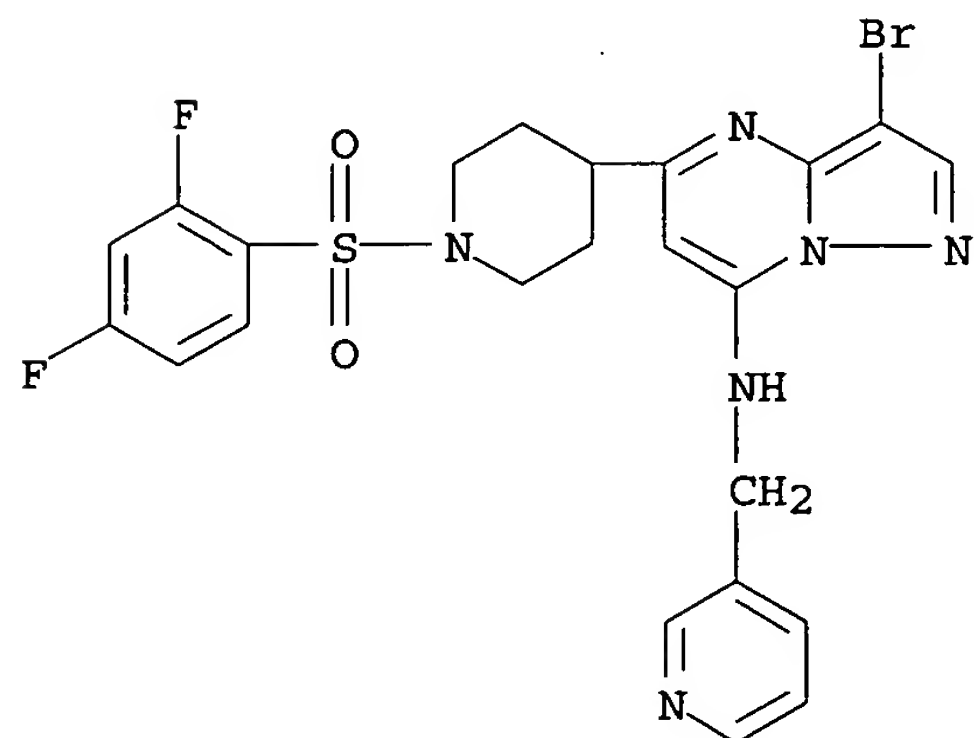
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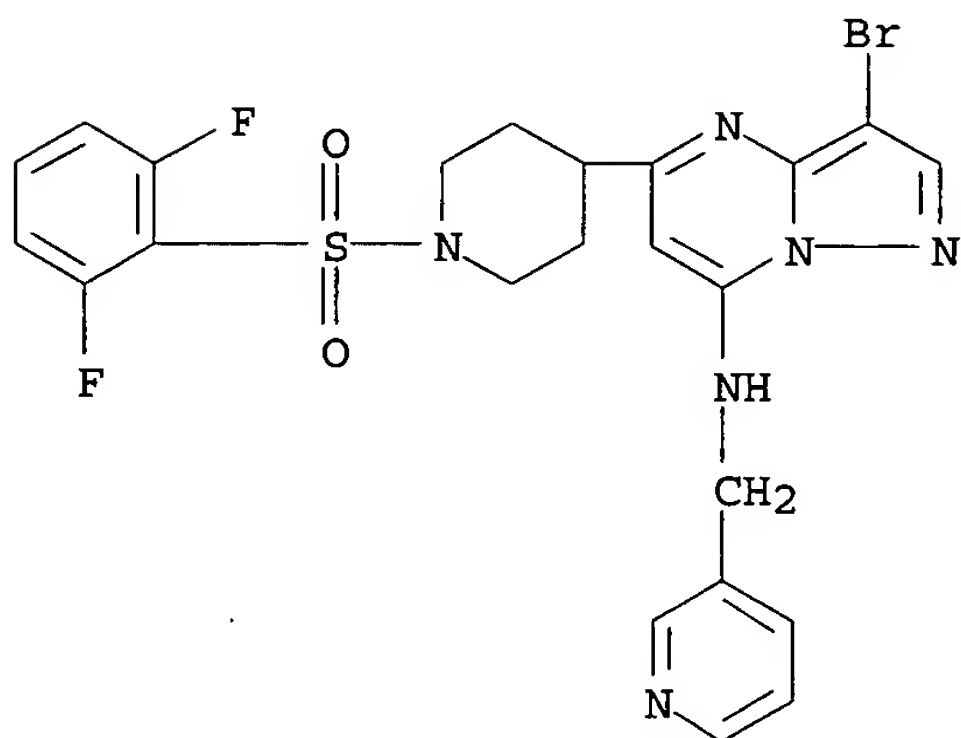


RN 677793-48-5 HCAPLUS  
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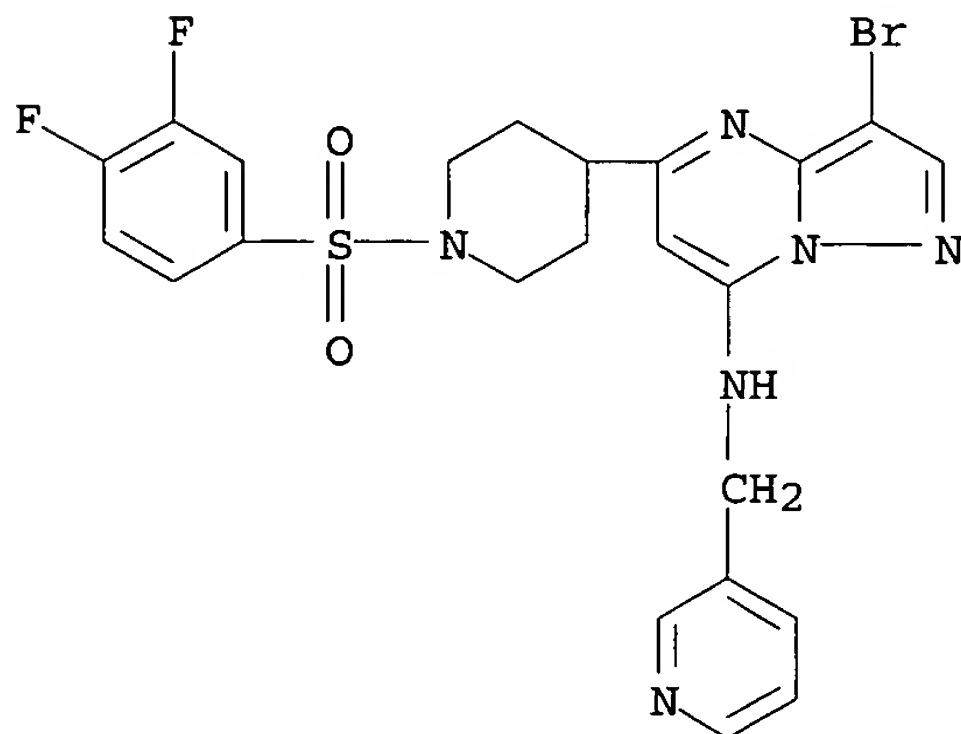
RN 677793-49-6 HCAPLUS

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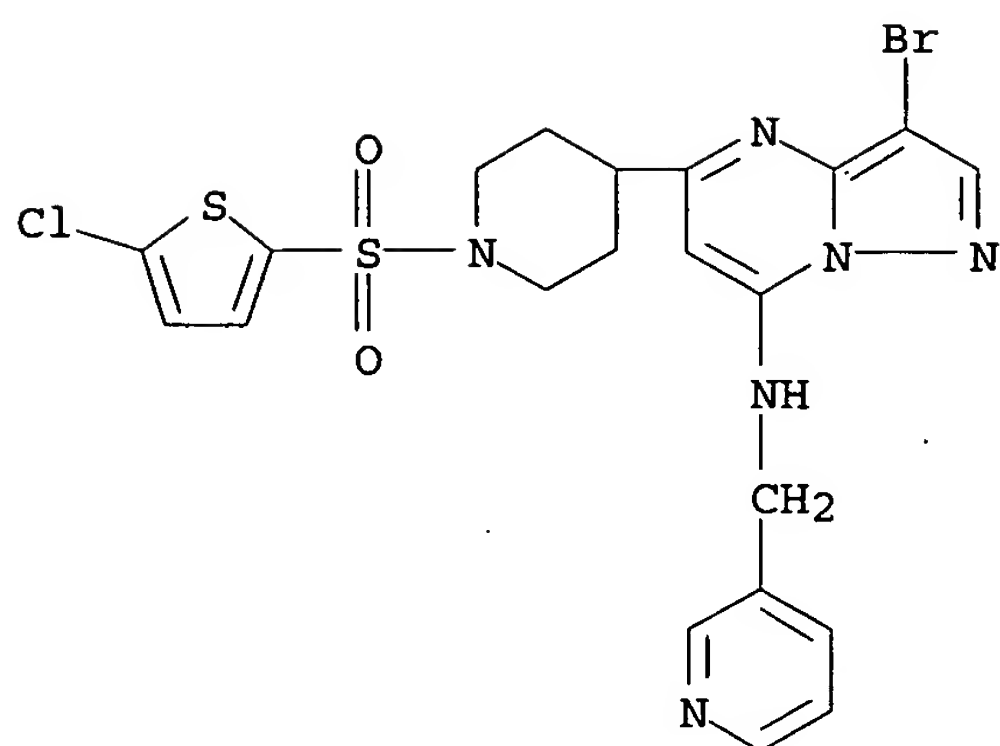
RN 677793-50-9 HCAPLUS

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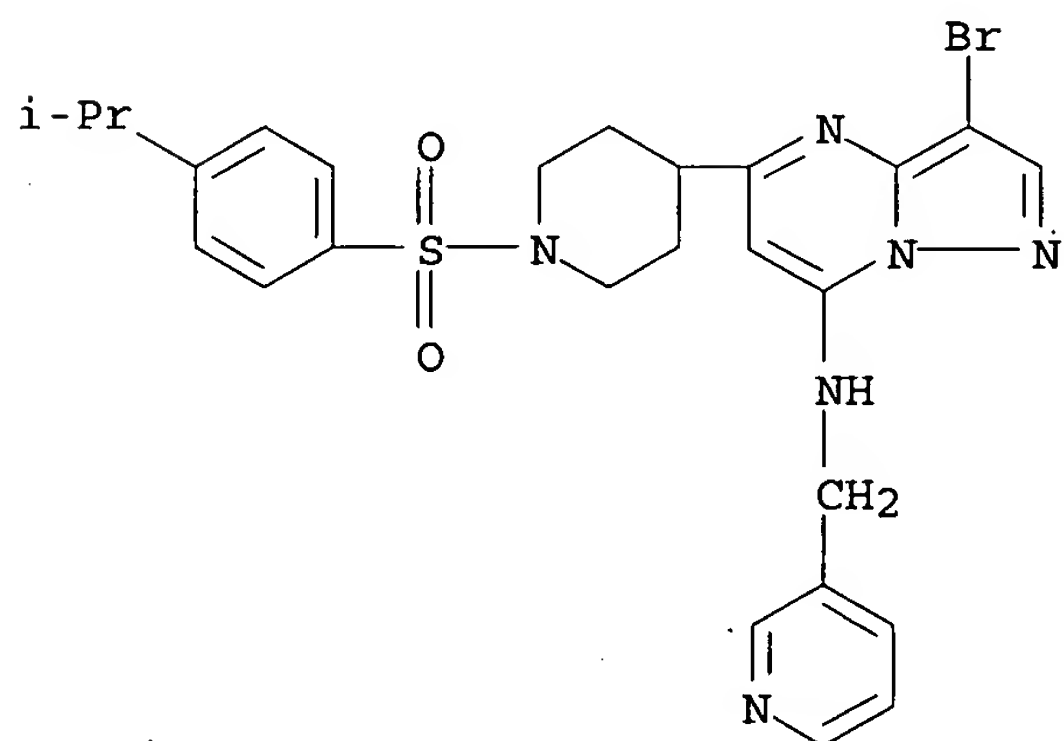


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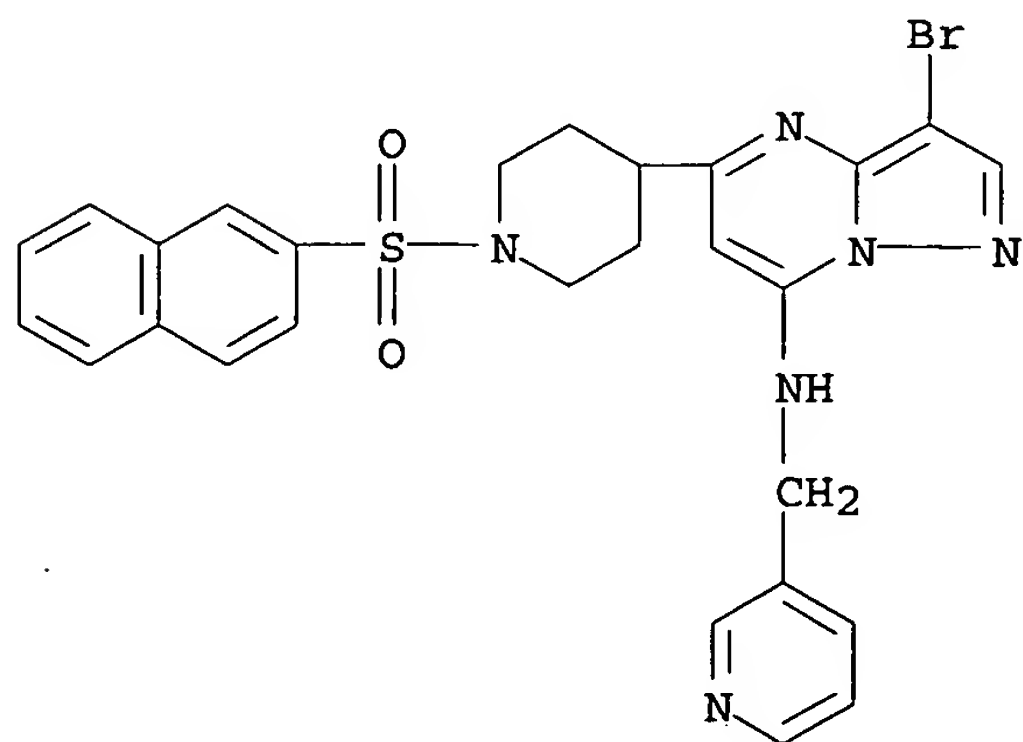
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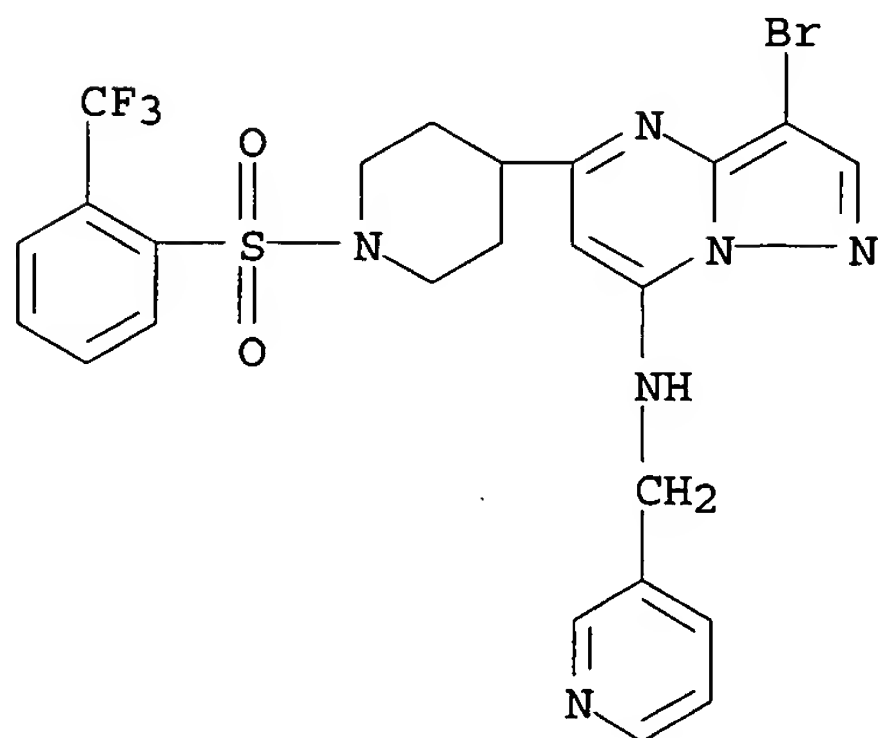
RN 677793-52-1 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1-methylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



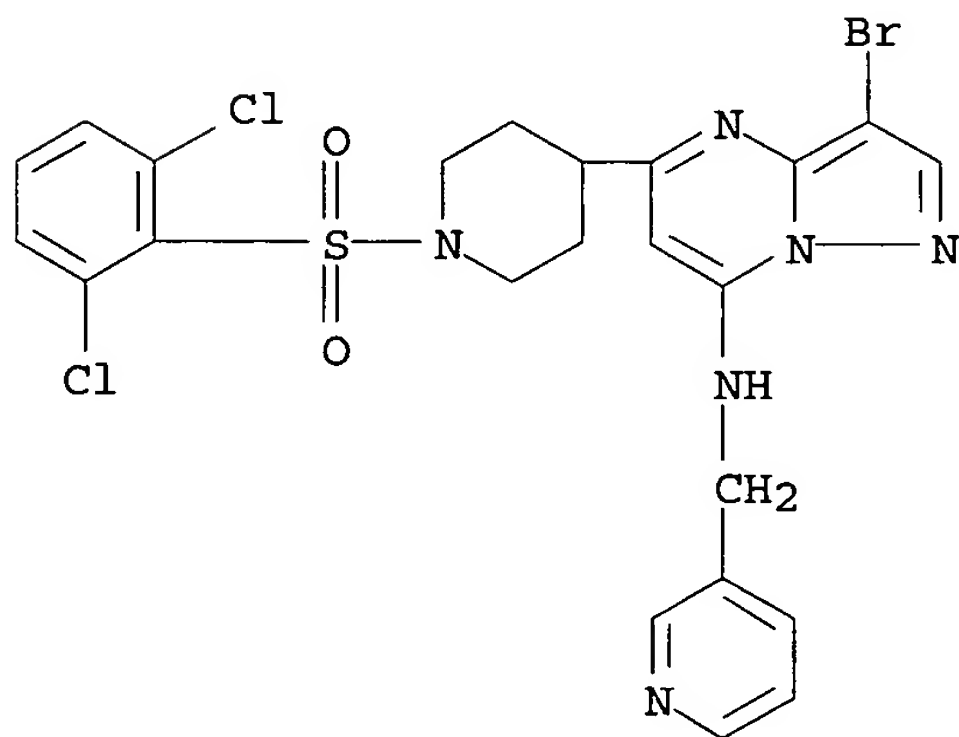
RN 677793-53-2 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 677793-54-3 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

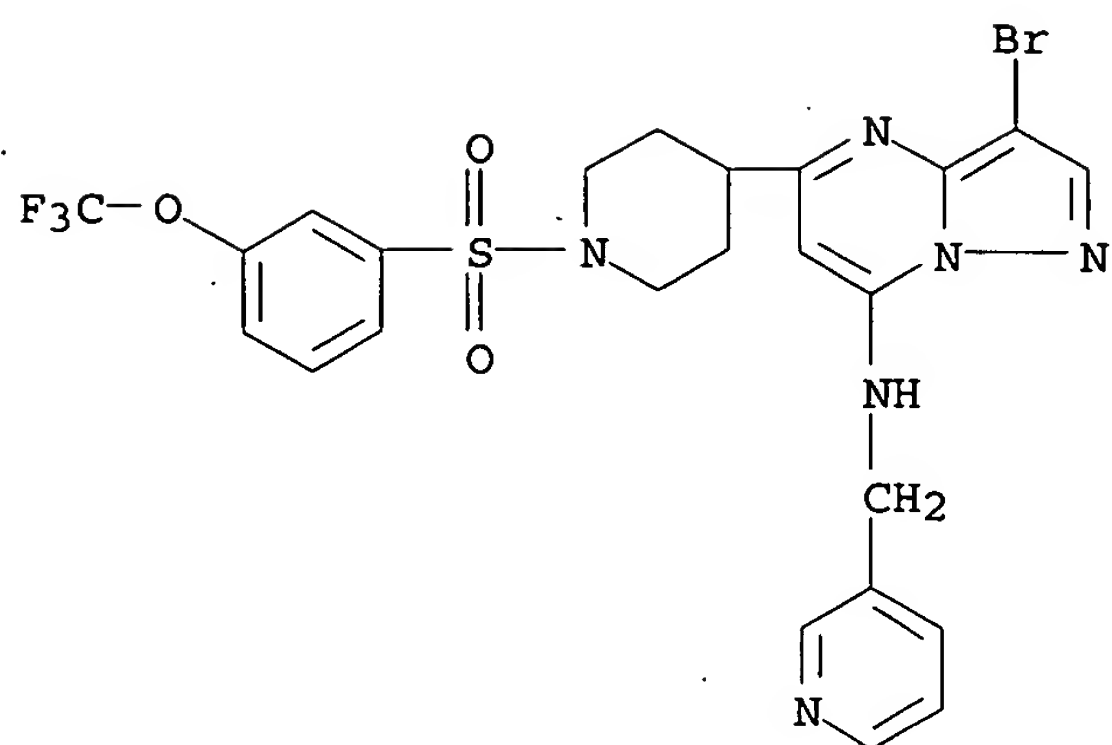


RN 677793-55-4 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



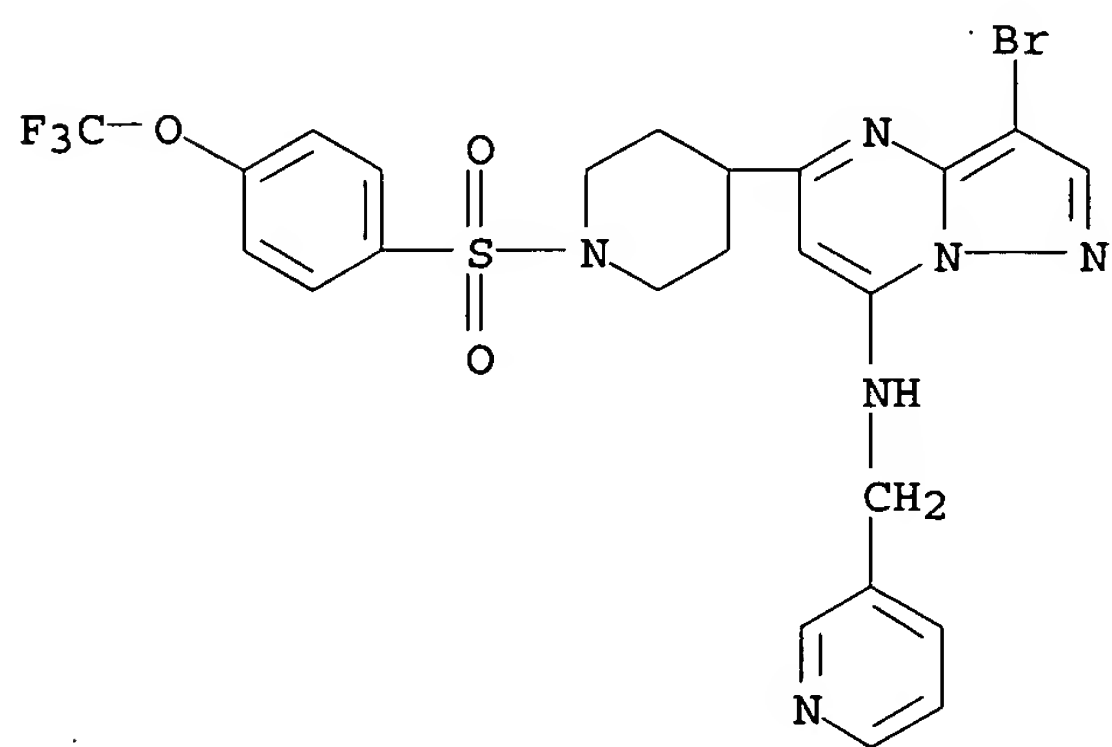
RN 677793-56-5 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)





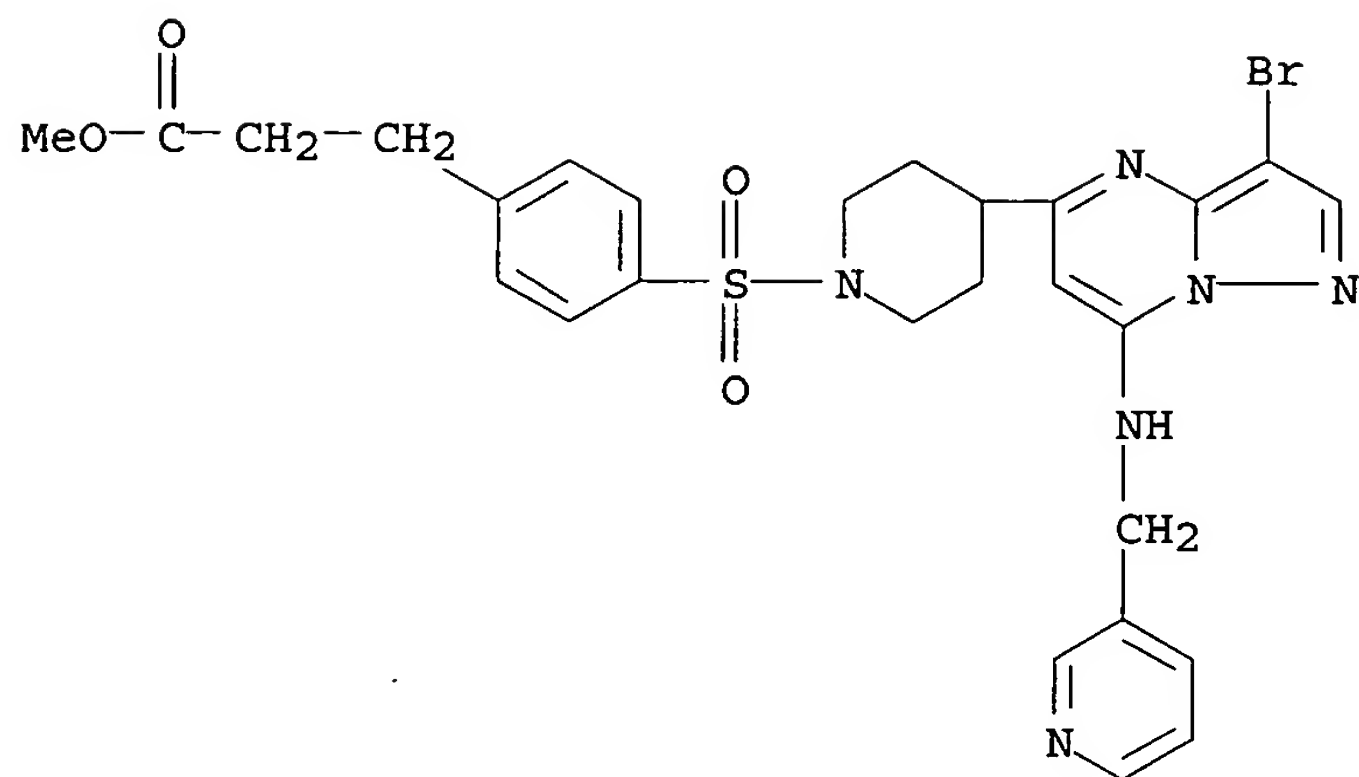
RN 677793-57-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



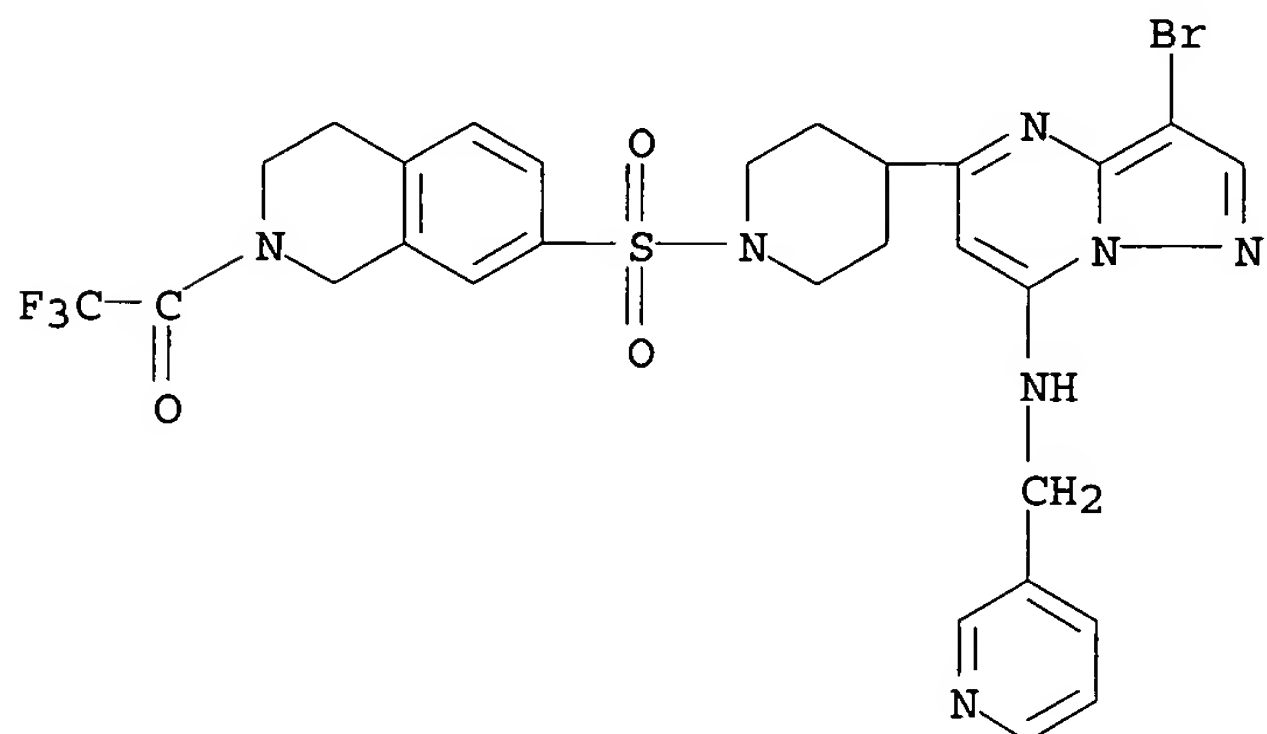
RN 677793-58-7 HCAPLUS

CN Benzenepropanoic acid, 4-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



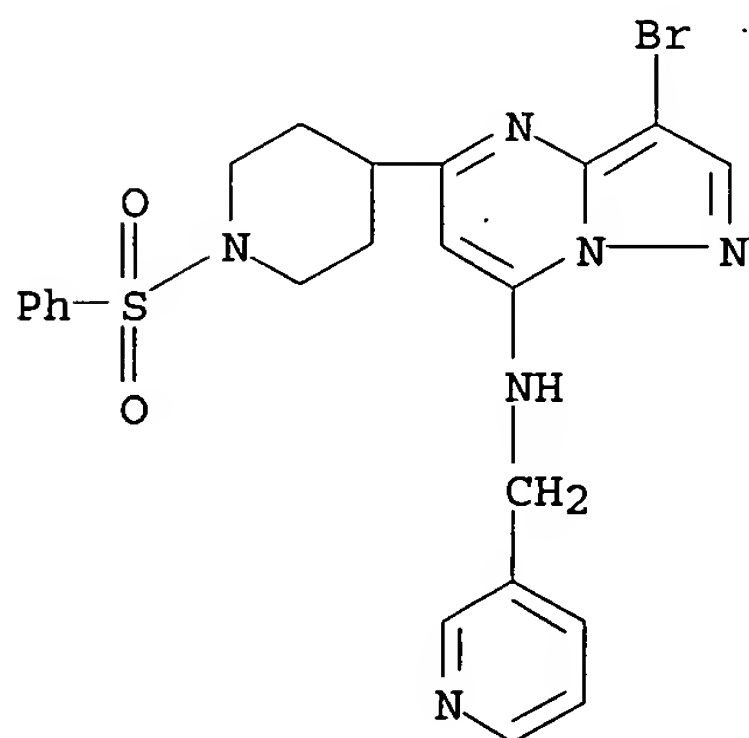
RN 677793-59-8 HCAPLUS

CN Isoquinoline, 7-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-1,2,3,4-tetrahydro-2-(trifluoroacetyl)- (9CI) (CA INDEX NAME)



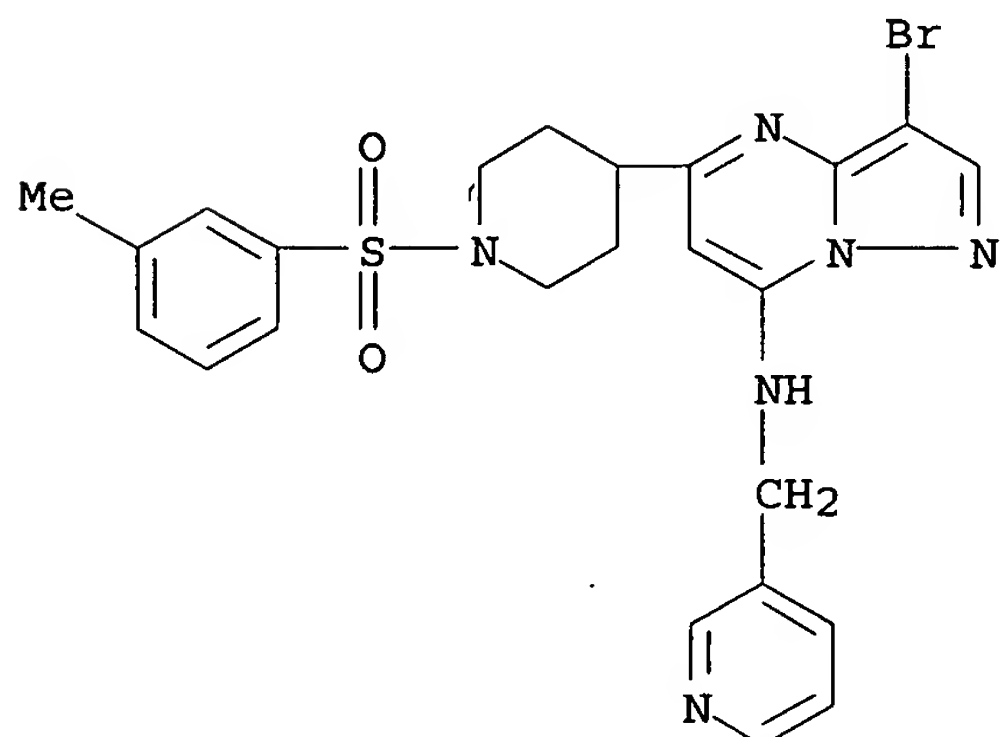
RN 677793-60-1 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



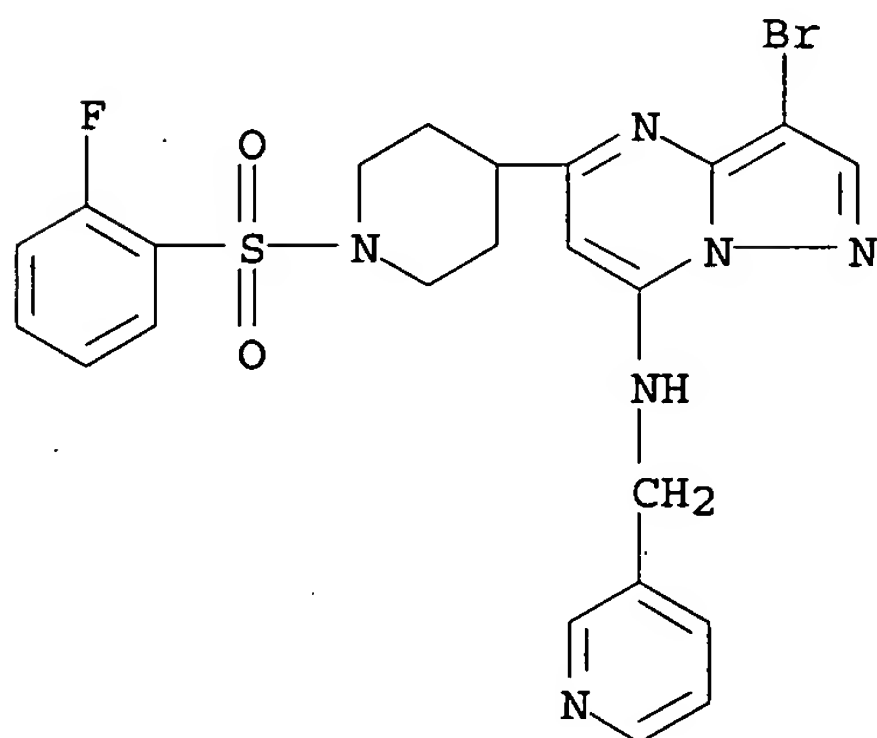
RN 677793-61-2 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



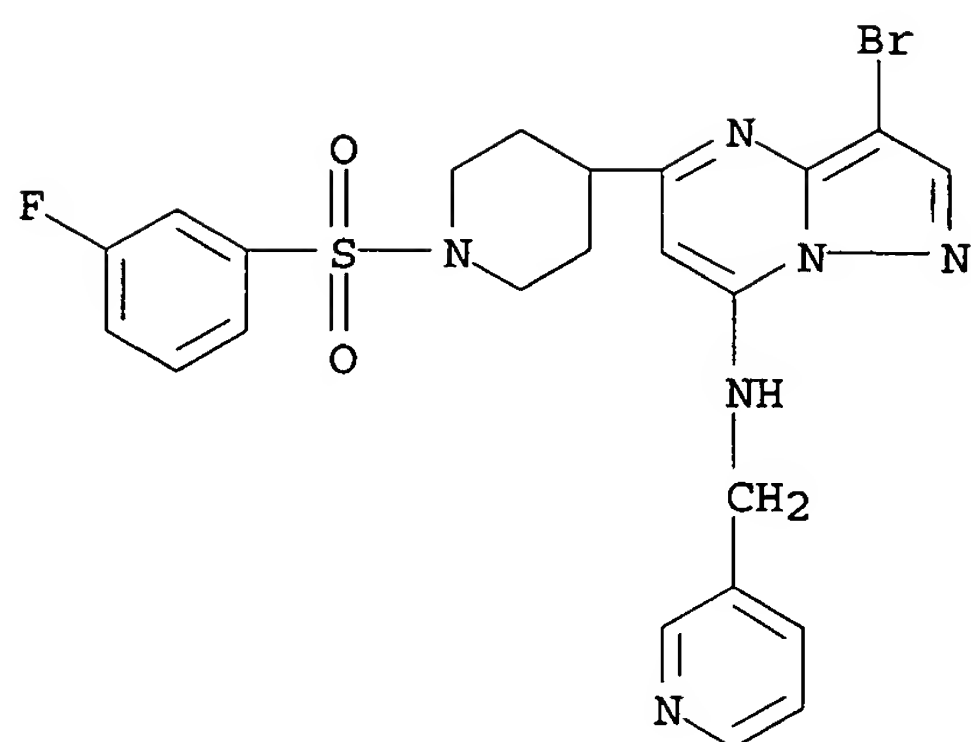
RN 677793-62-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



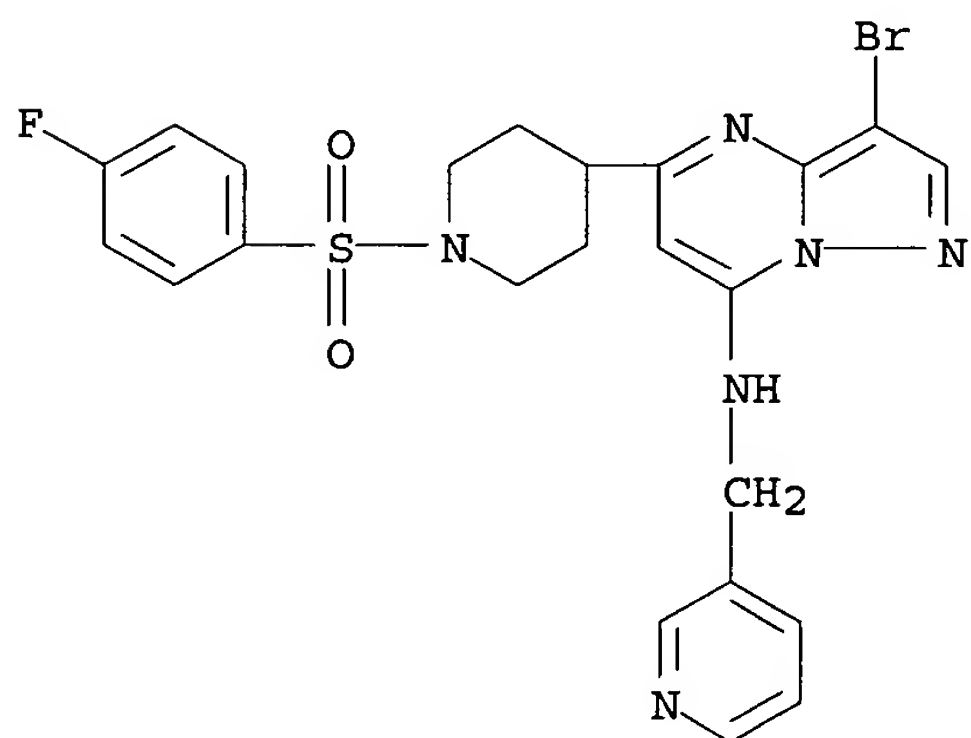
RN 677793-63-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



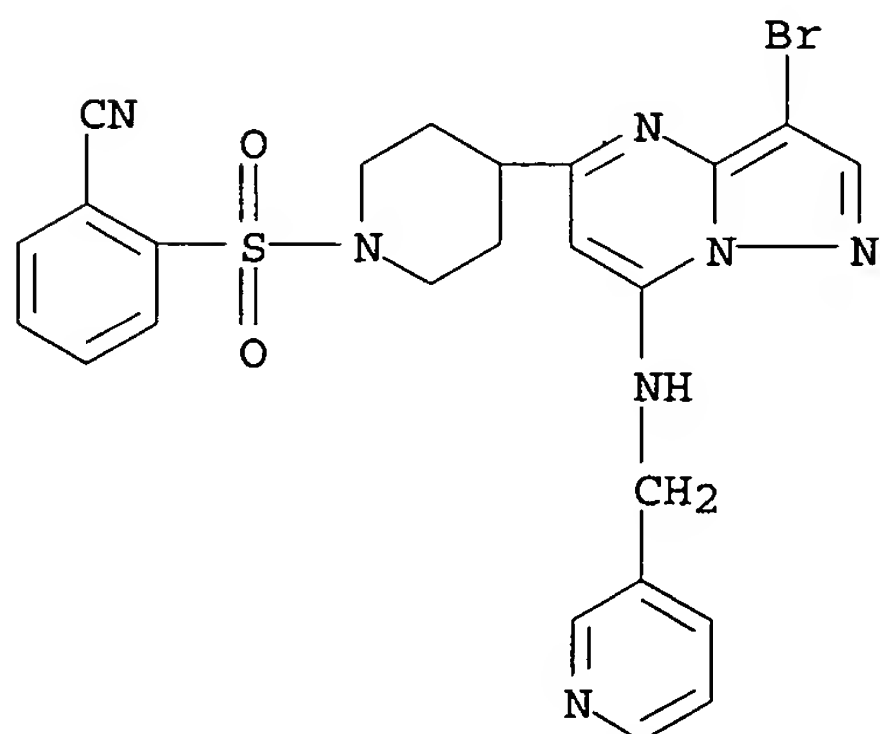
RN 677793-64-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



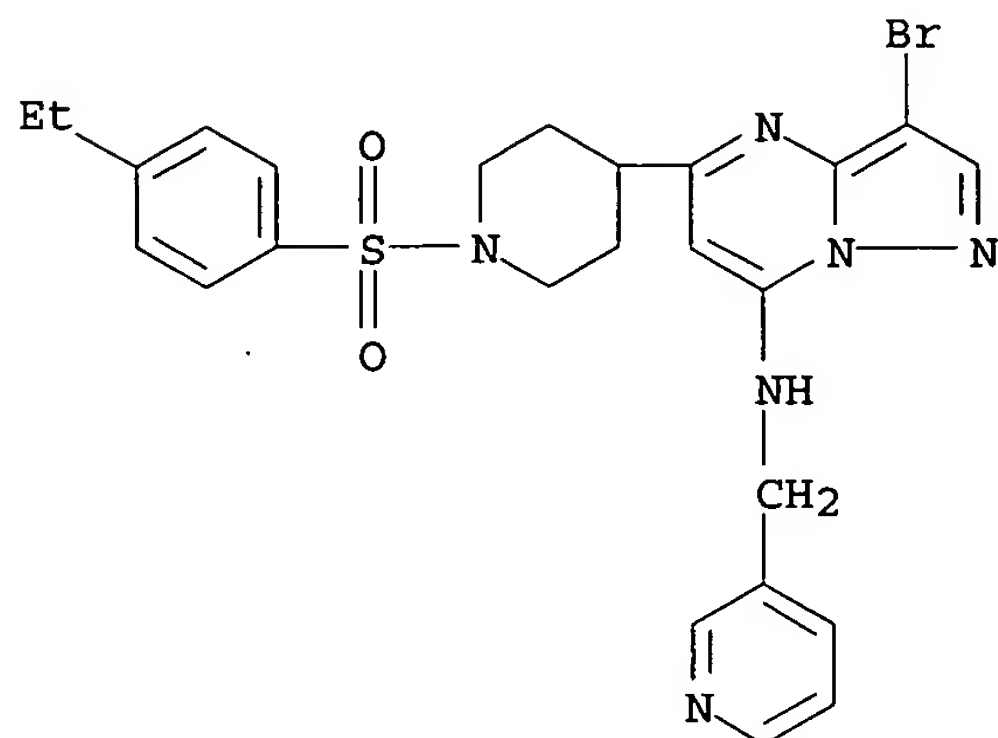
RN 677793-65-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



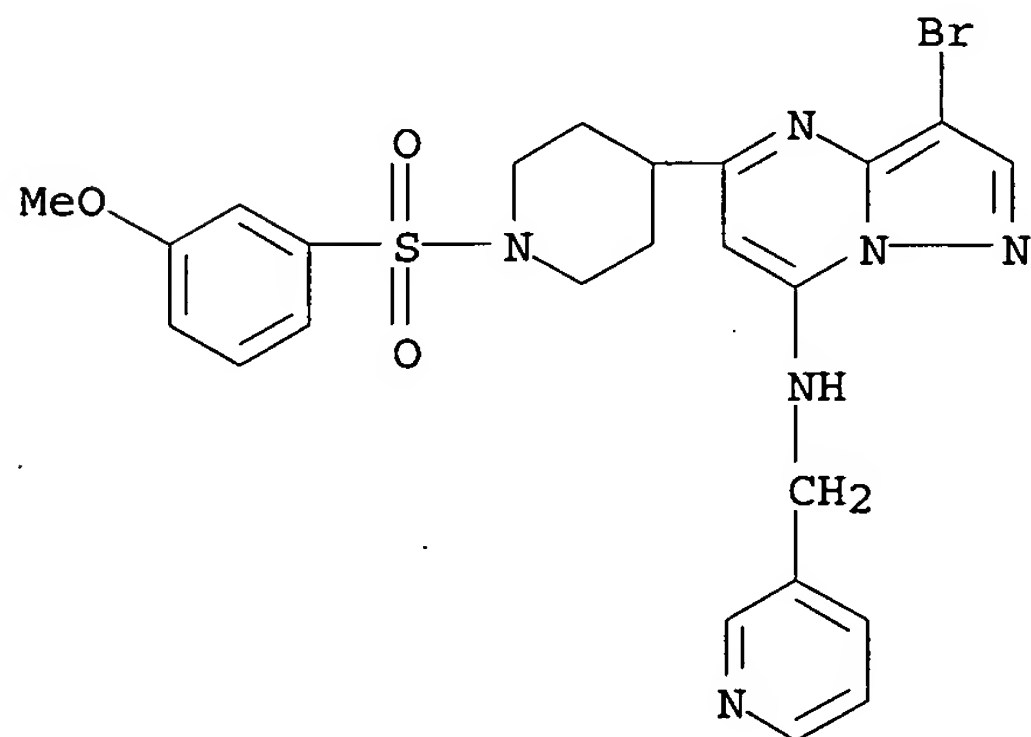
RN 677793-66-7 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-ethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



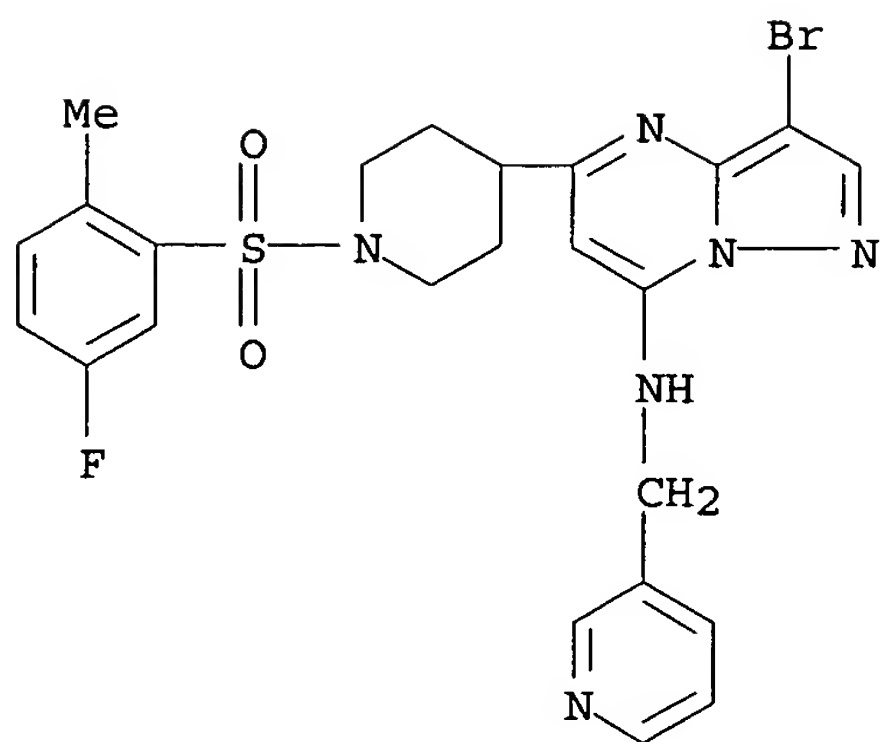
RN 677793-67-8 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



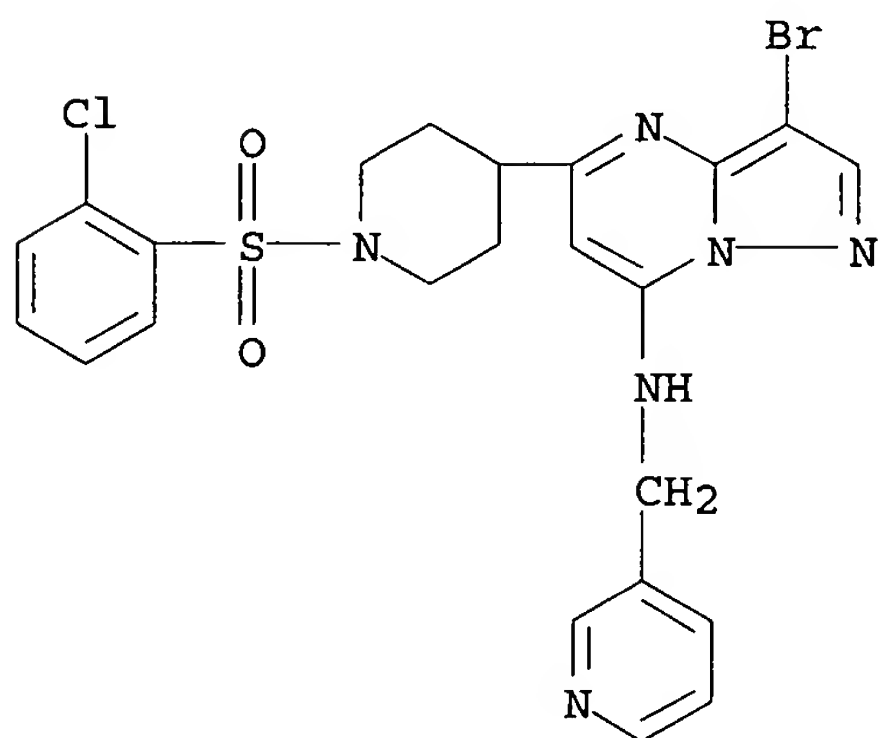
RN 677793-68-9 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-fluoro-2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



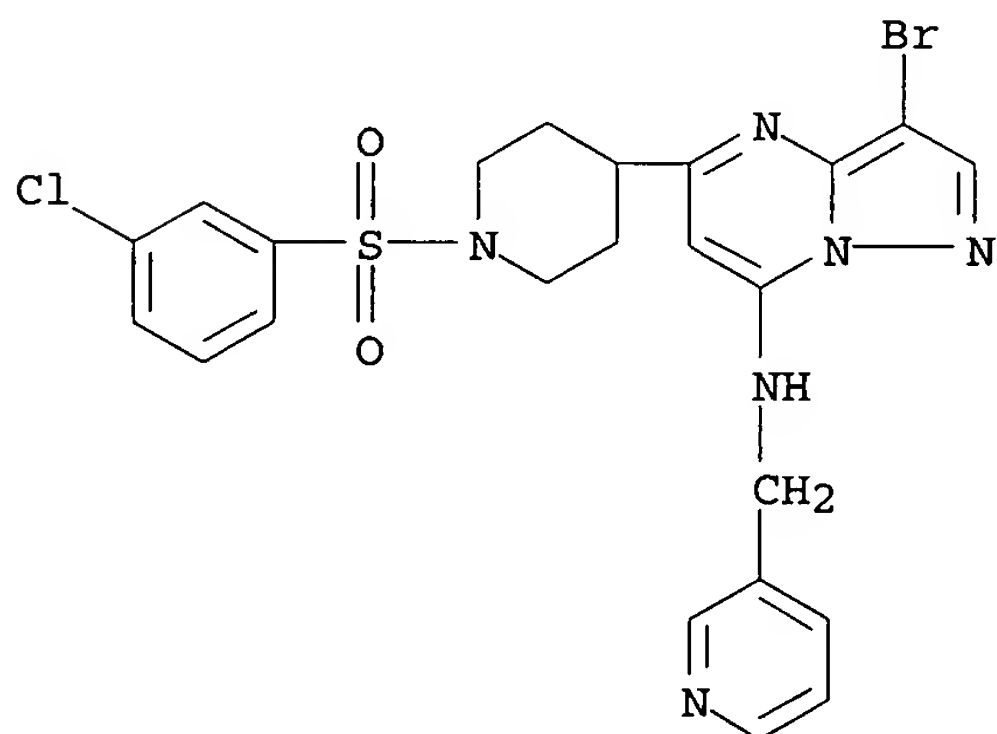
RN 677793-69-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



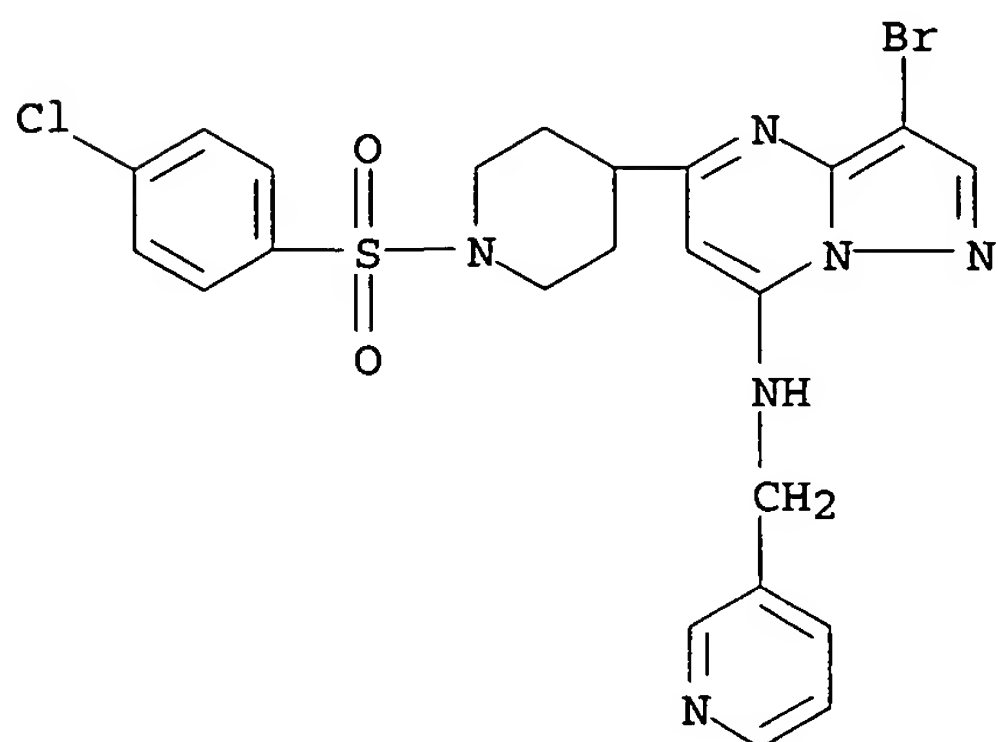
RN 677793-70-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



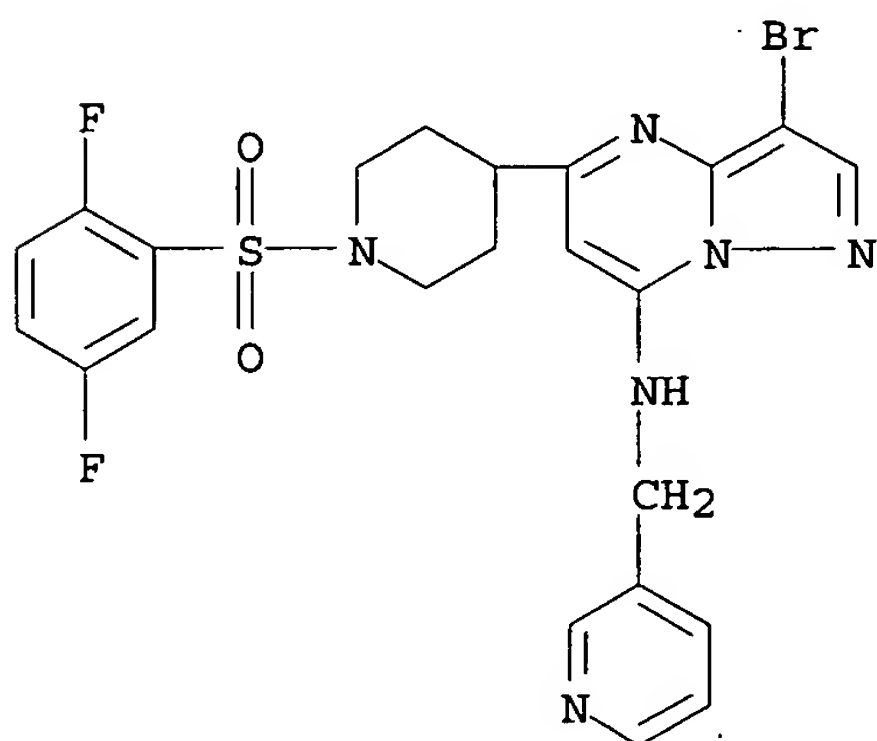
RN 677793-71-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



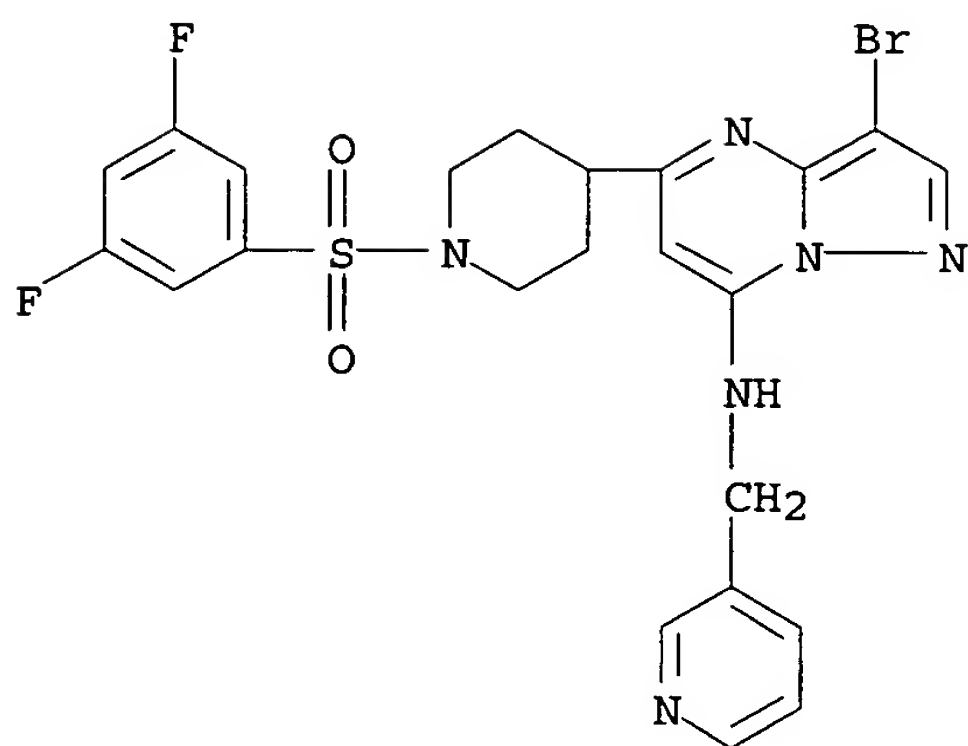
RN 677793-72-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



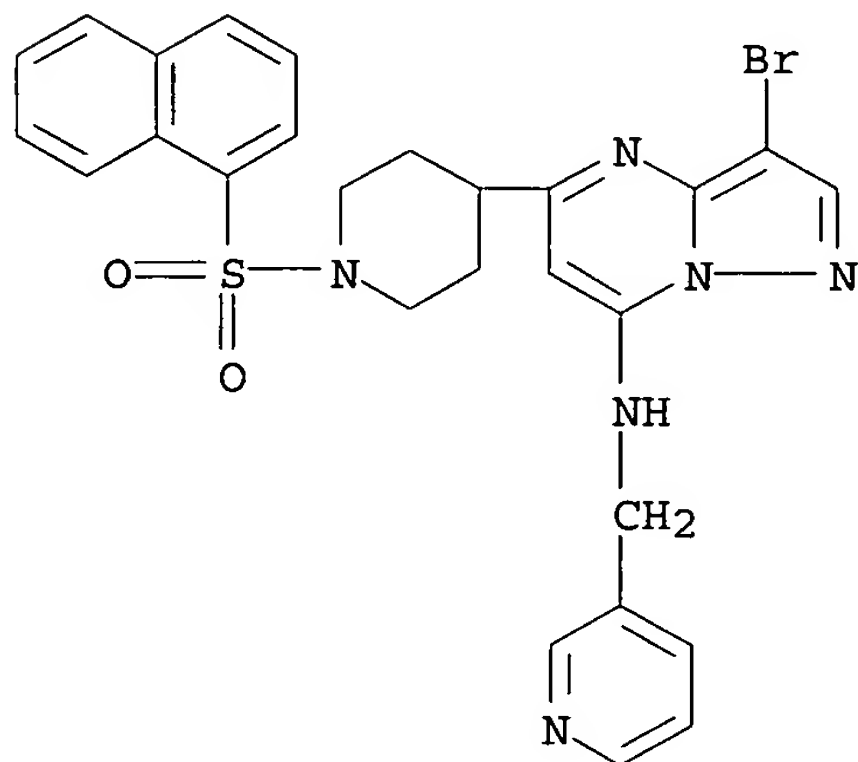
RN 677793-73-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



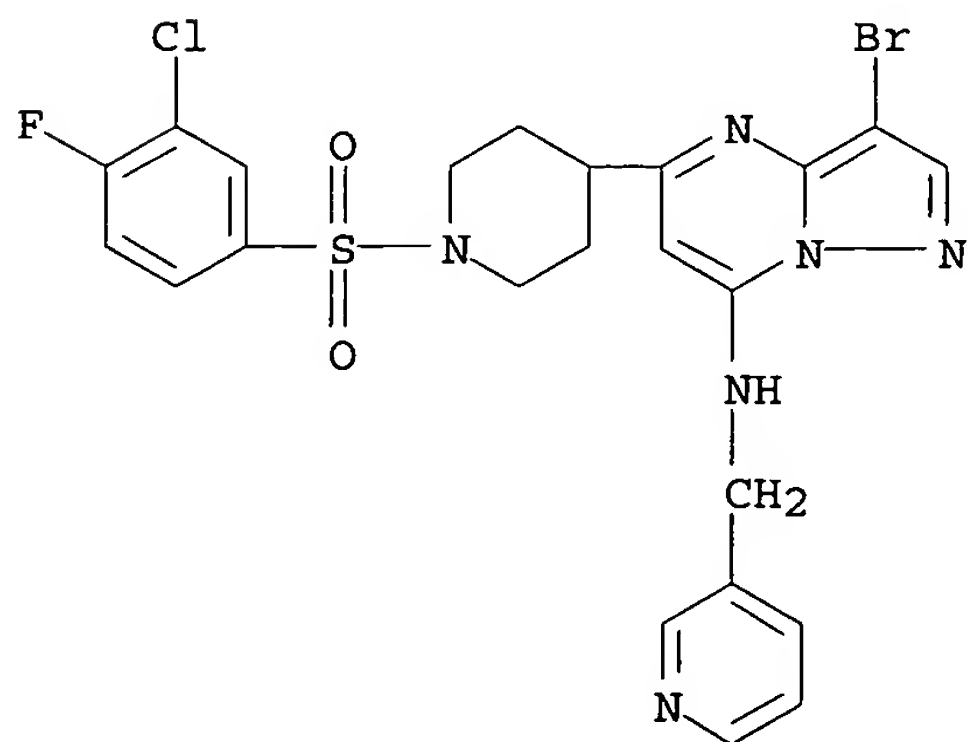
RN 677793-74-7 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 677793-75-8 HCAPLUS

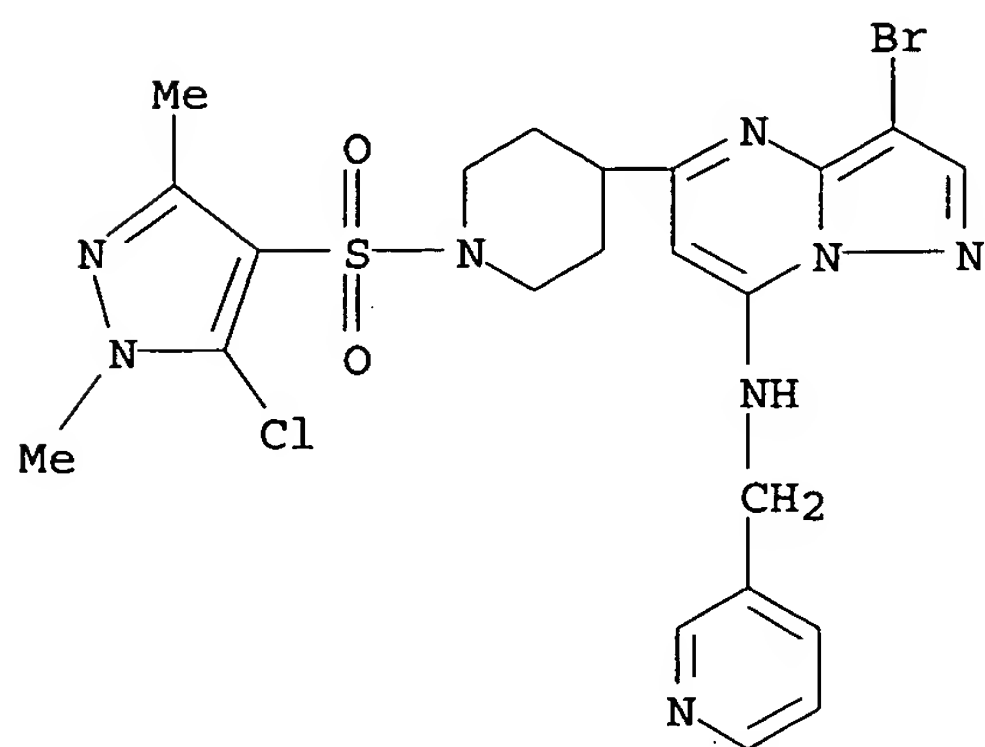
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)





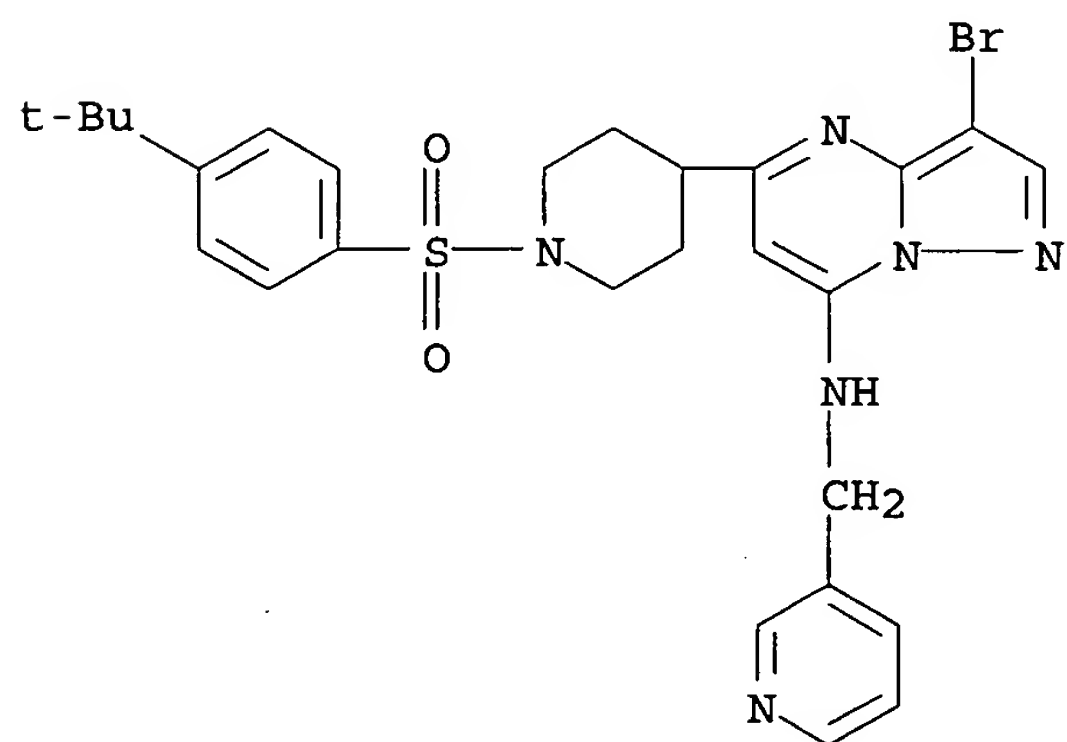
RN 677793-76-9 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)



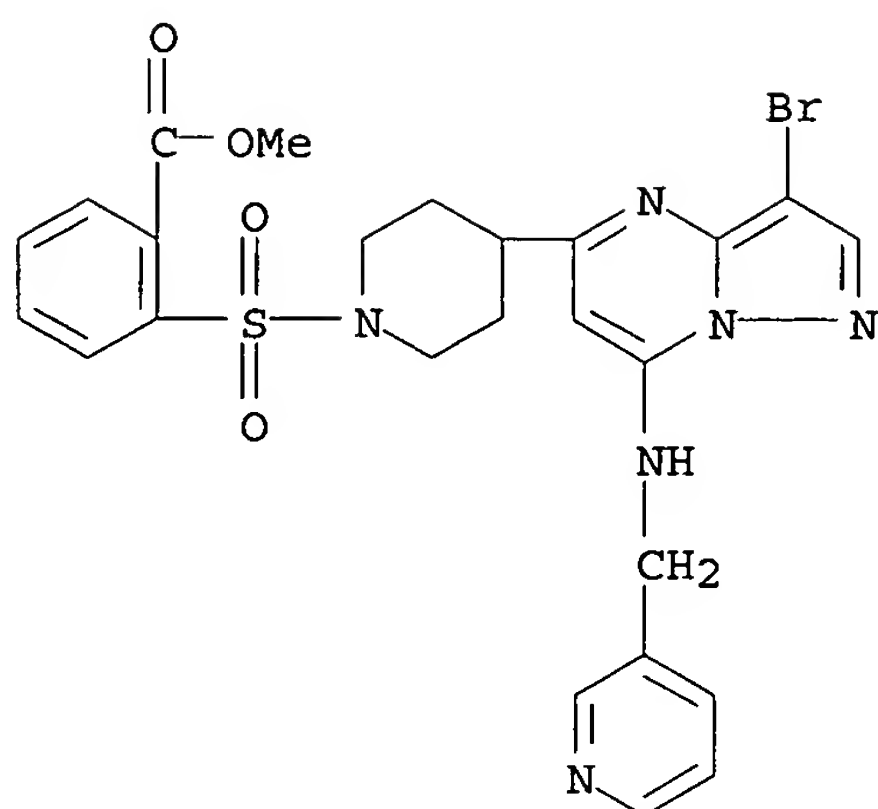
RN 677793-77-0 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



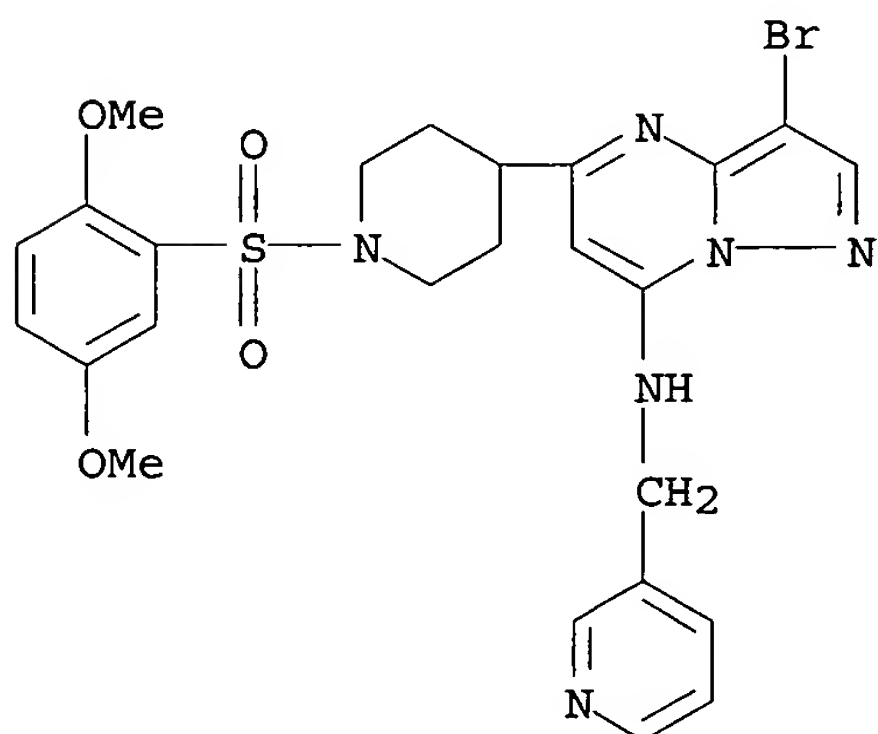
RN 677793-78-1 HCAPLUS

CN Benzoic acid, 2-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



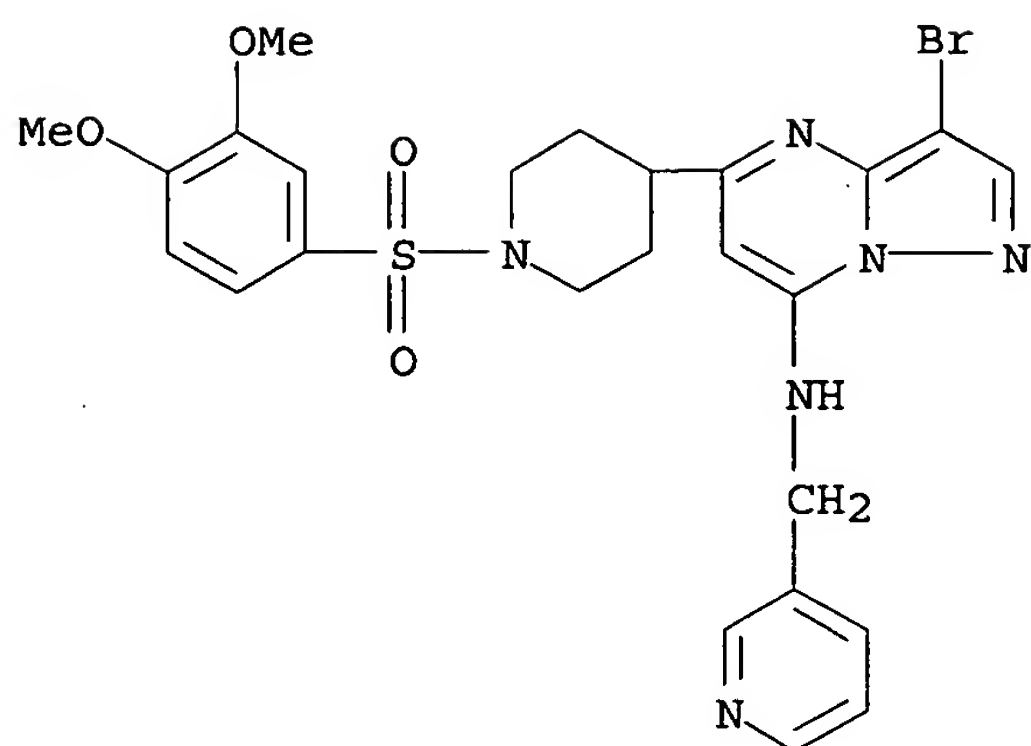
RN 677793-79-2 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



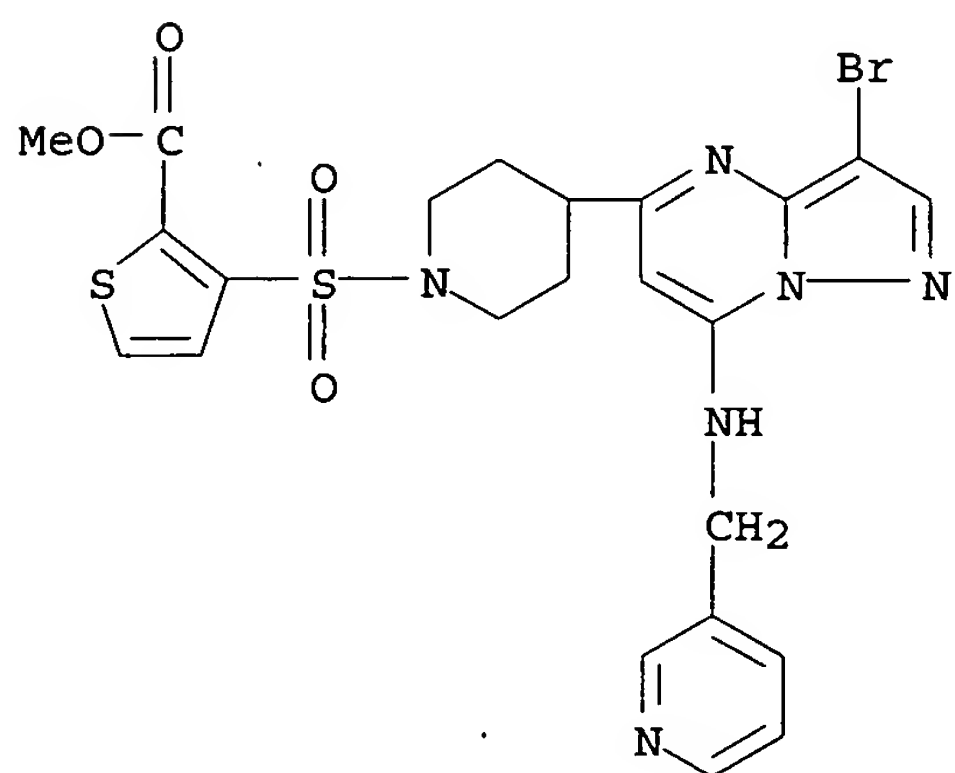
RN 677793-80-5 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



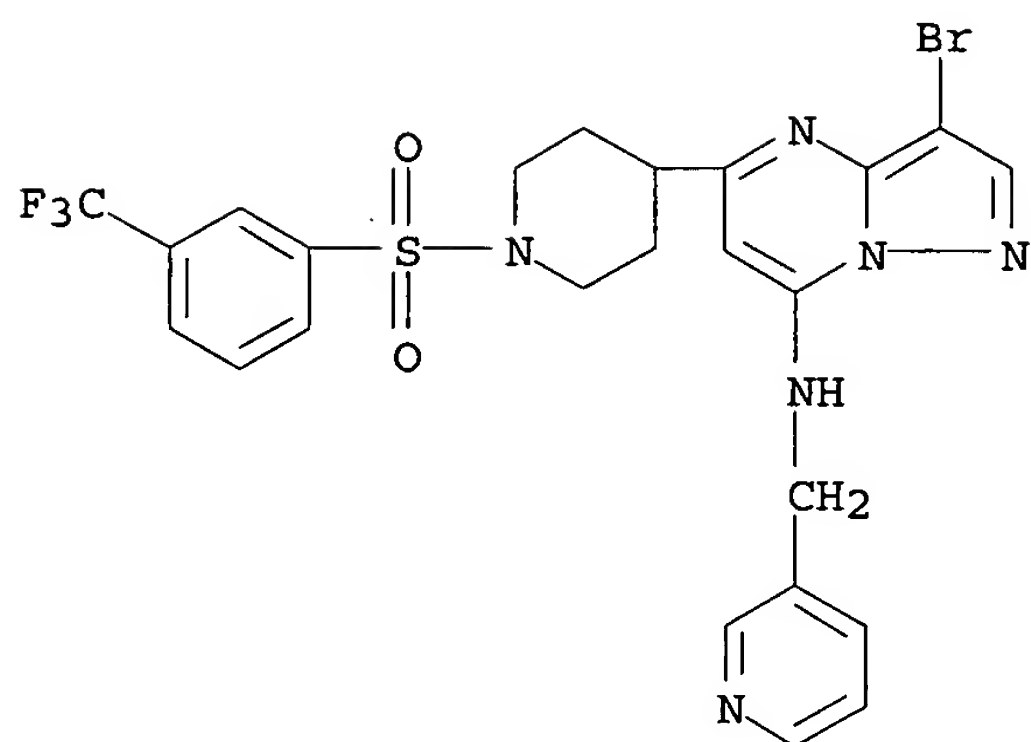
RN 677793-81-6 HCAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

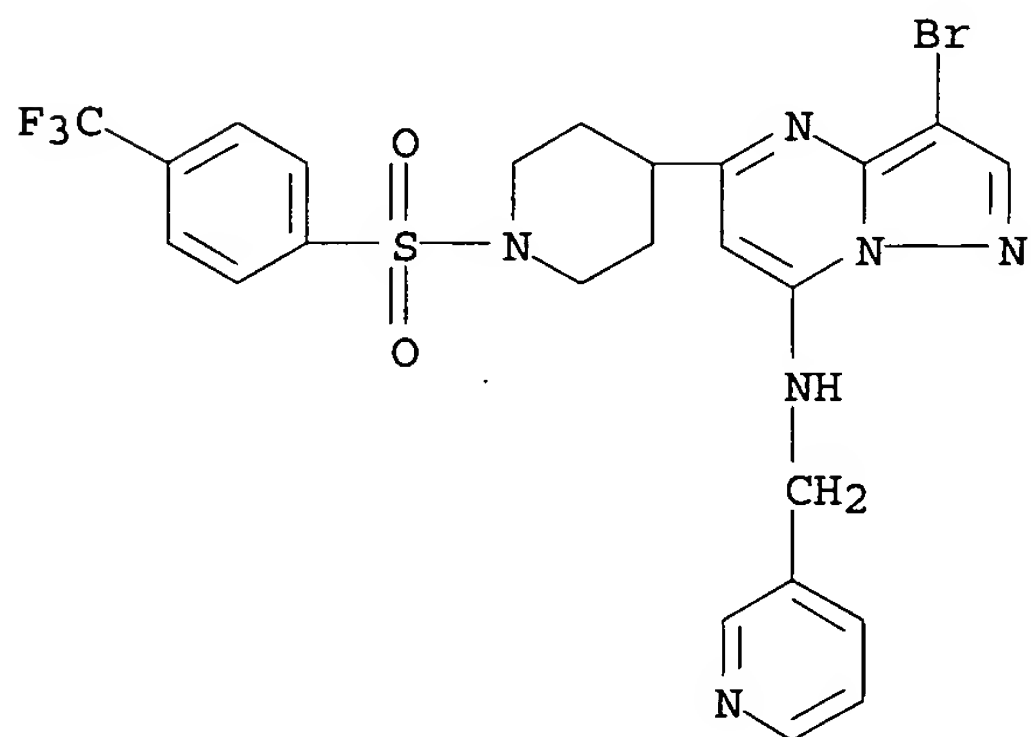


RN 677793-82-7 HCAPLUS

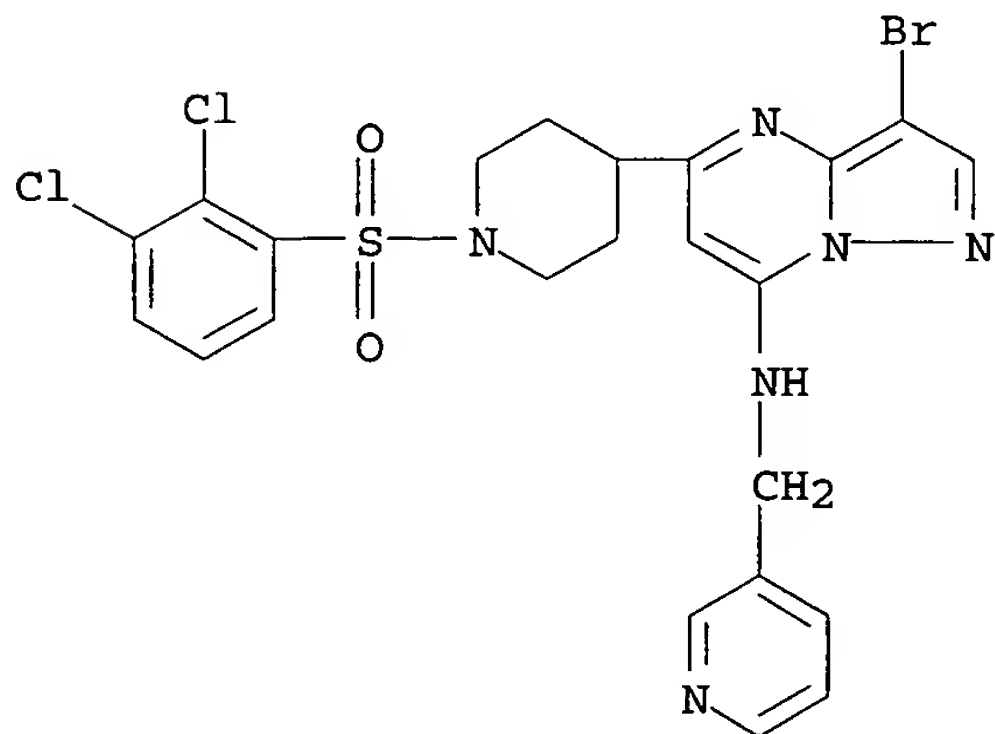
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



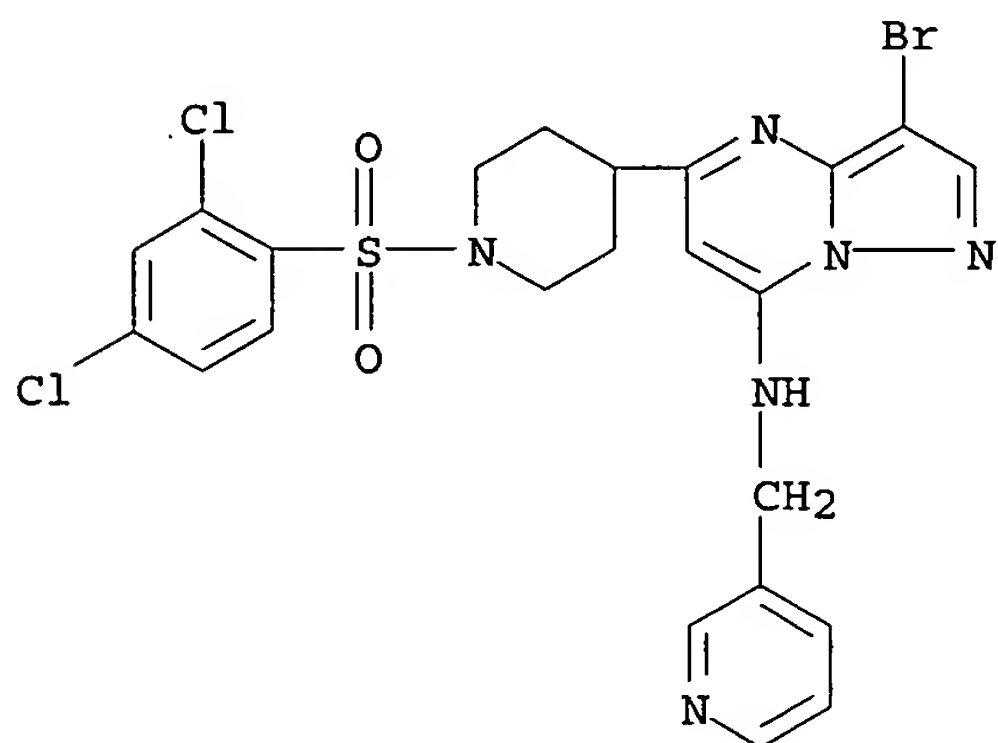
RN 677793-83-8 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



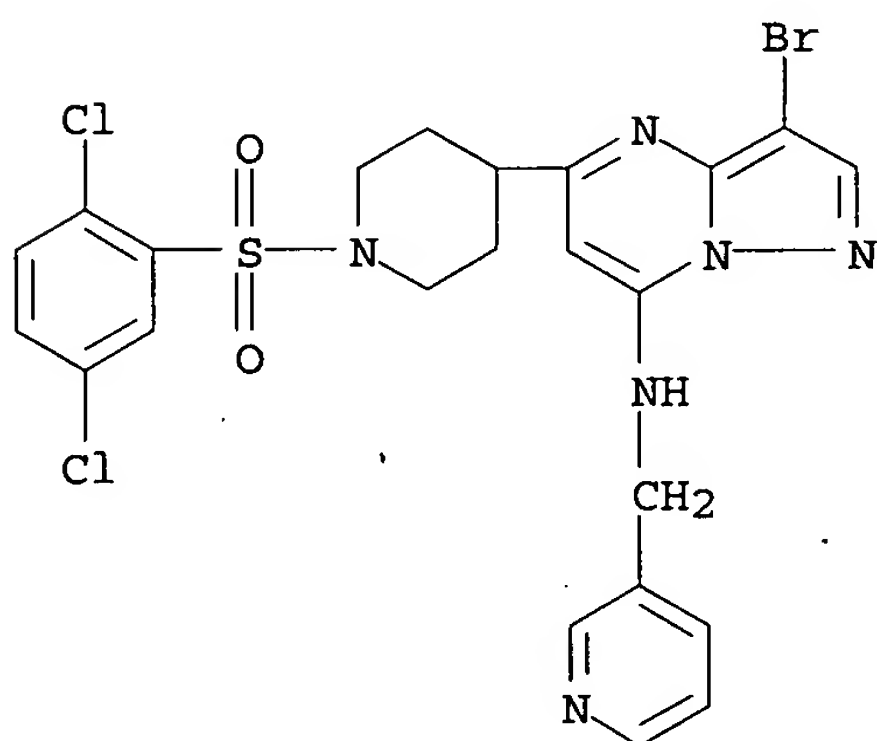
RN 677793-84-9 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



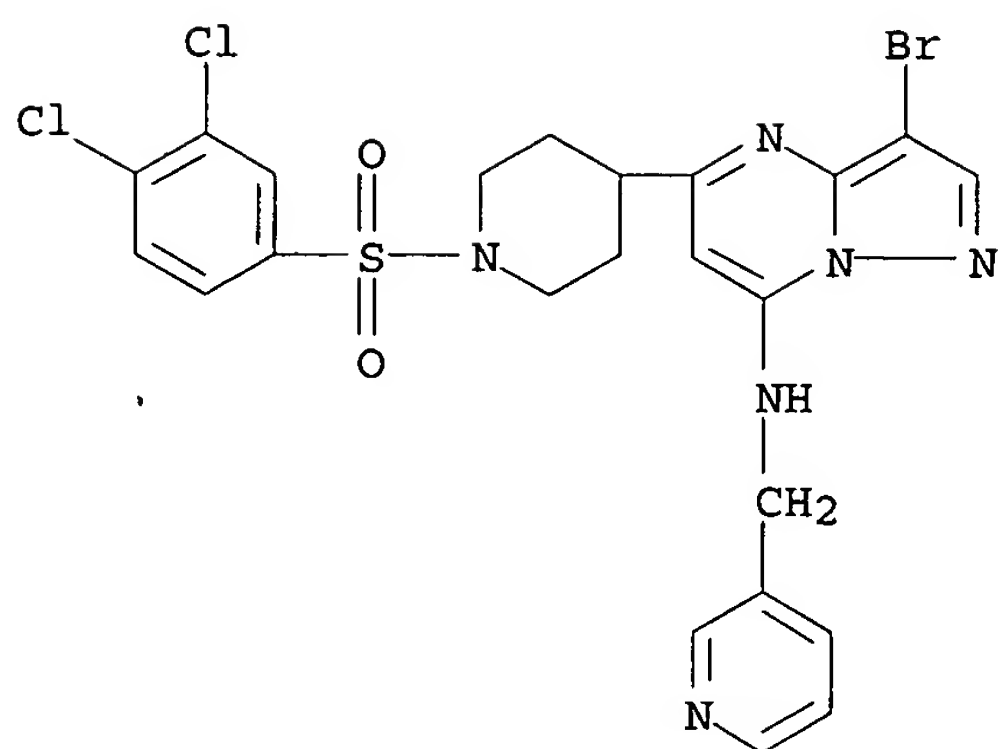
RN 677793-85-0 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-  
 alpyrimidin-5-yl]-1-[(2,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677793-86-1 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-  
 alpyrimidin-5-yl]-1-[(2,5-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

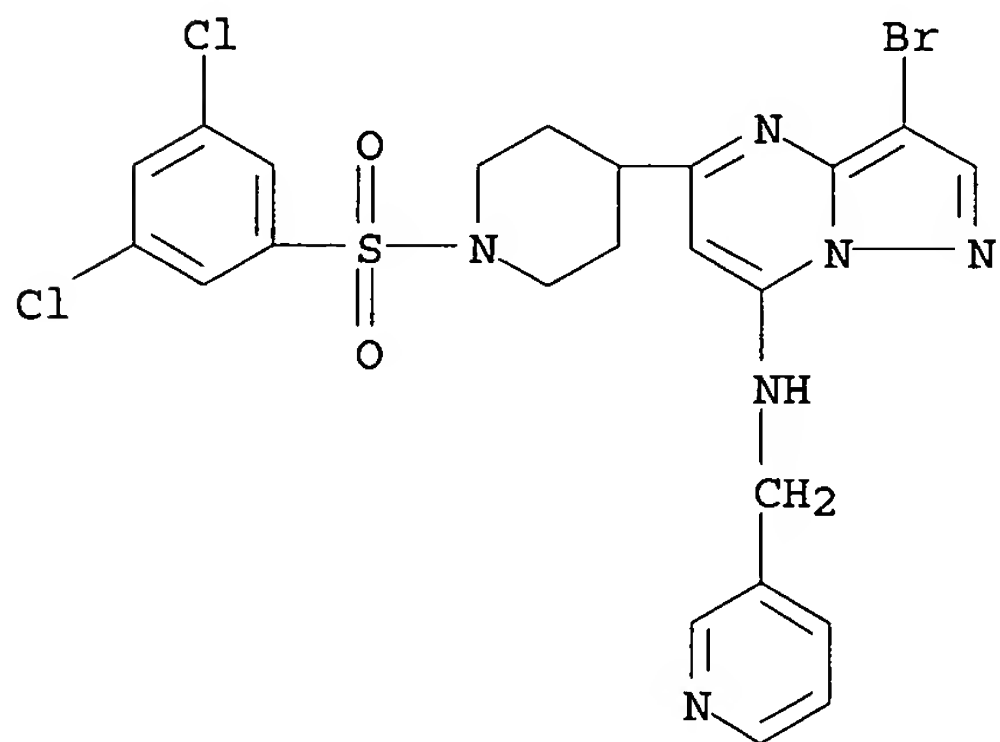


RN 677793-87-2 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-  
 alpyrimidin-5-yl]-1-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



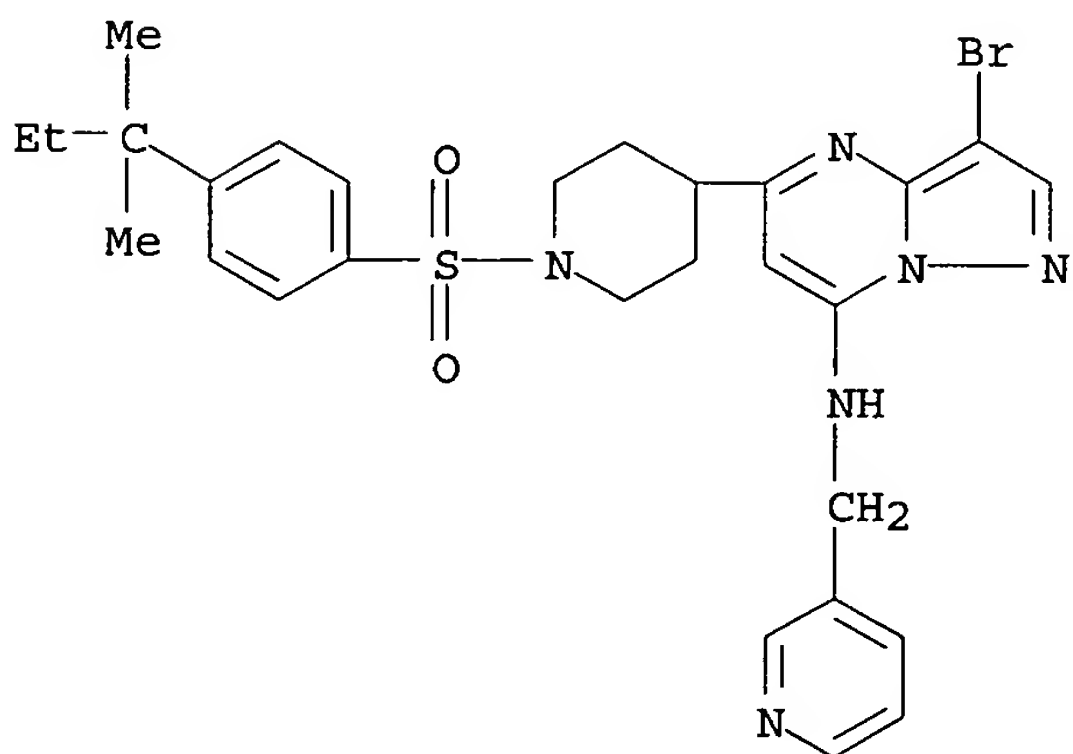
RN 677793-88-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

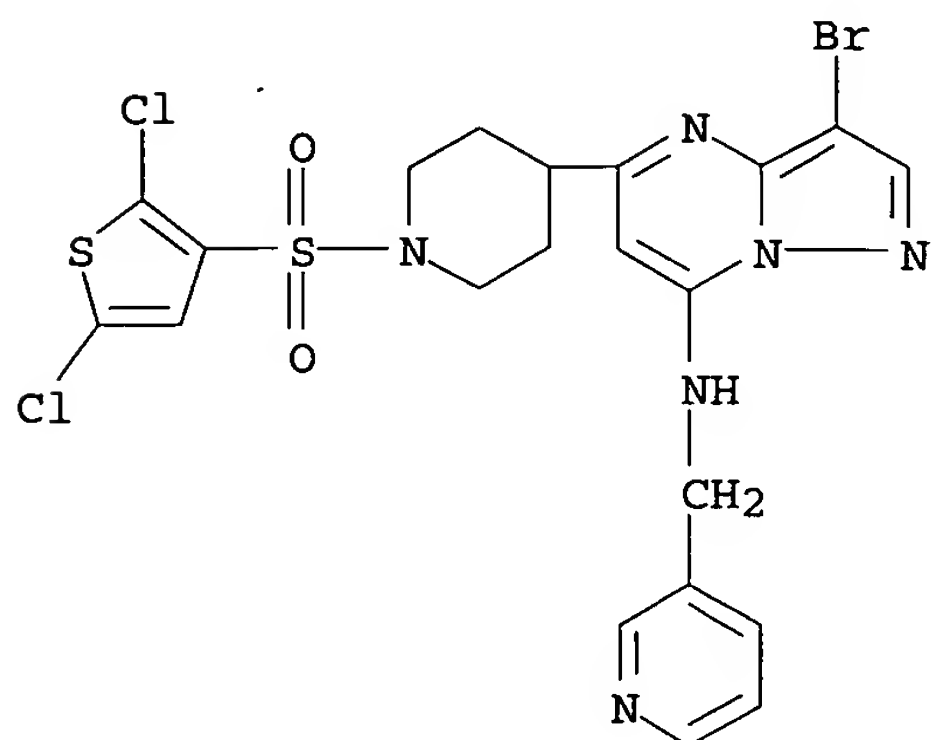


RN 677793-89-4 HCAPLUS

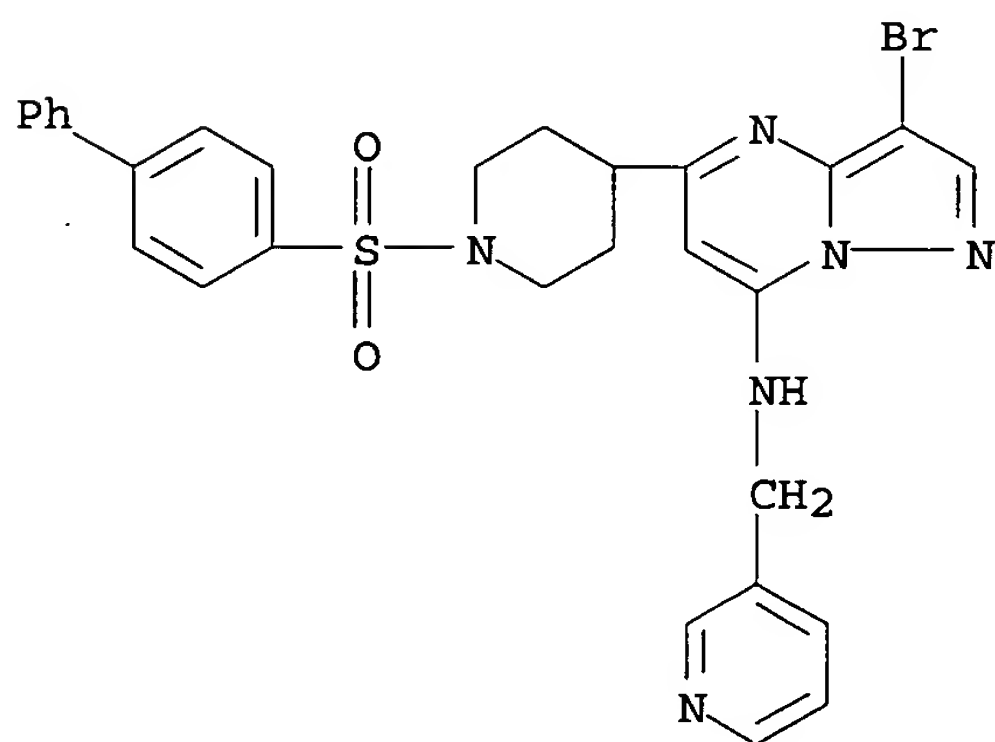
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylpropyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



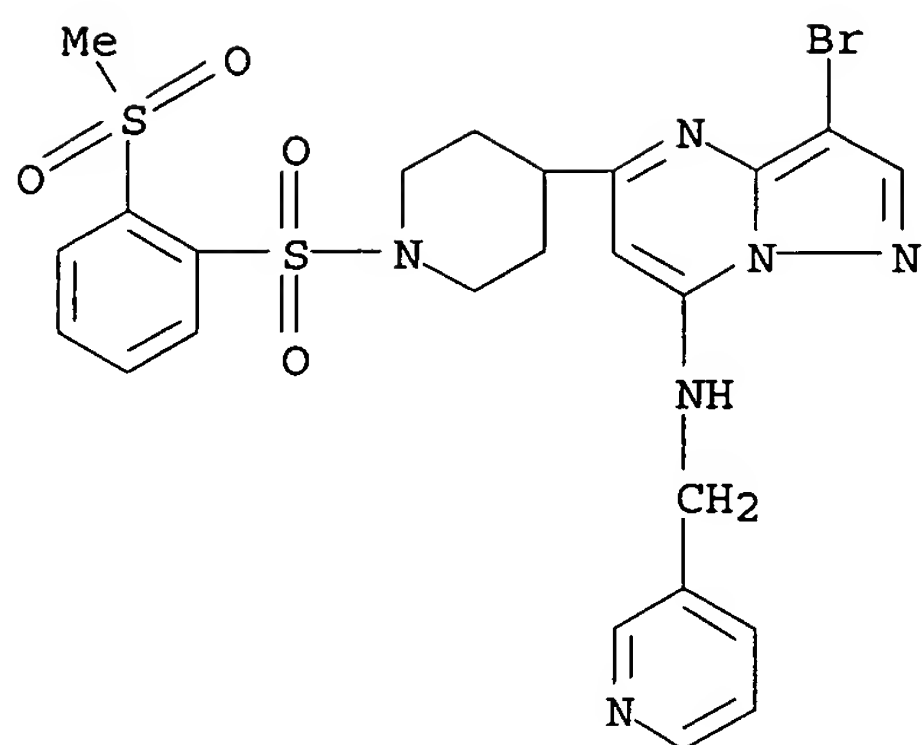
RN 677793-90-7 HCAPLUS  
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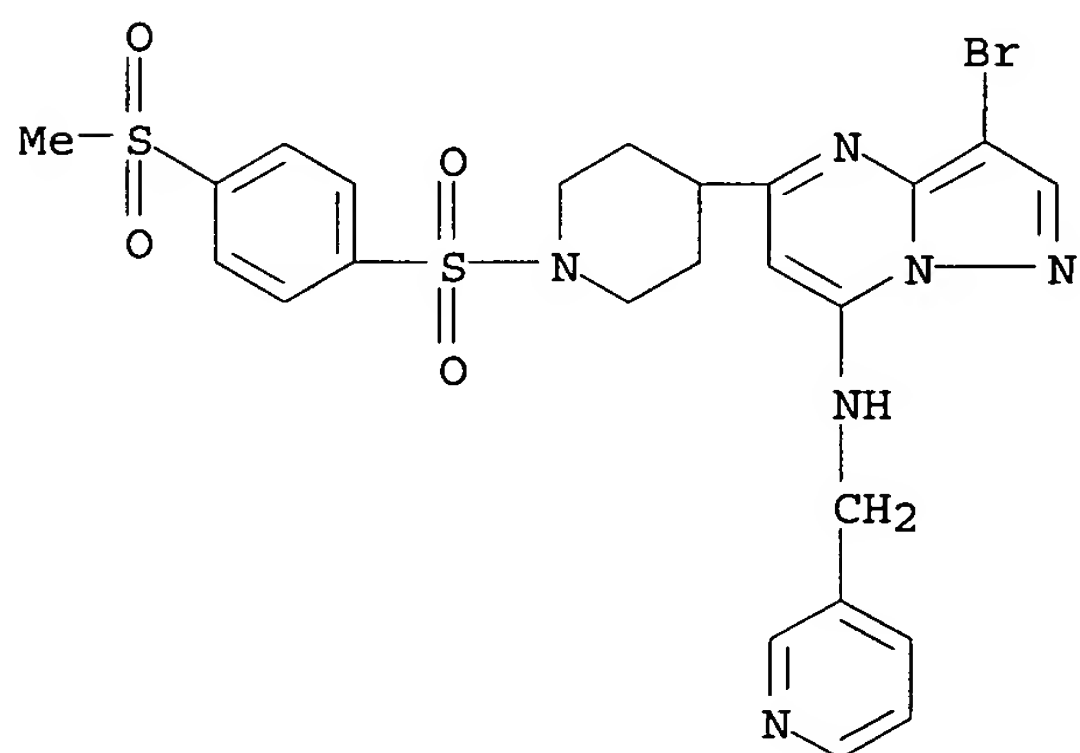
RN 677793-91-8 HCAPLUS  
 CN Piperidine, 1-([1,1'-biphenyl]-4-ylsulfonyl)-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 677793-92-9 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

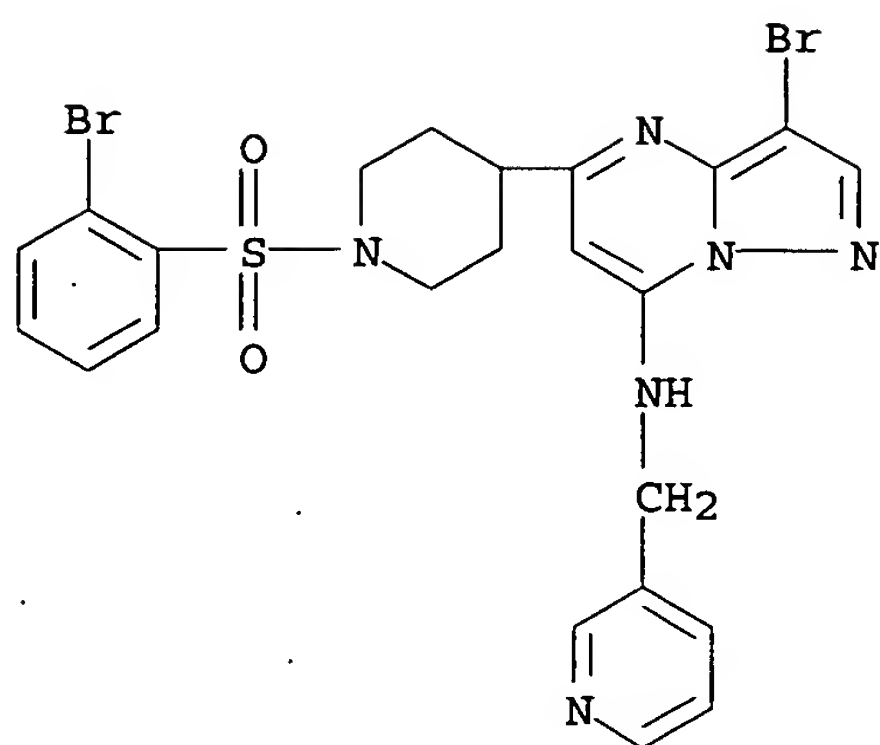


RN 677793-93-0 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



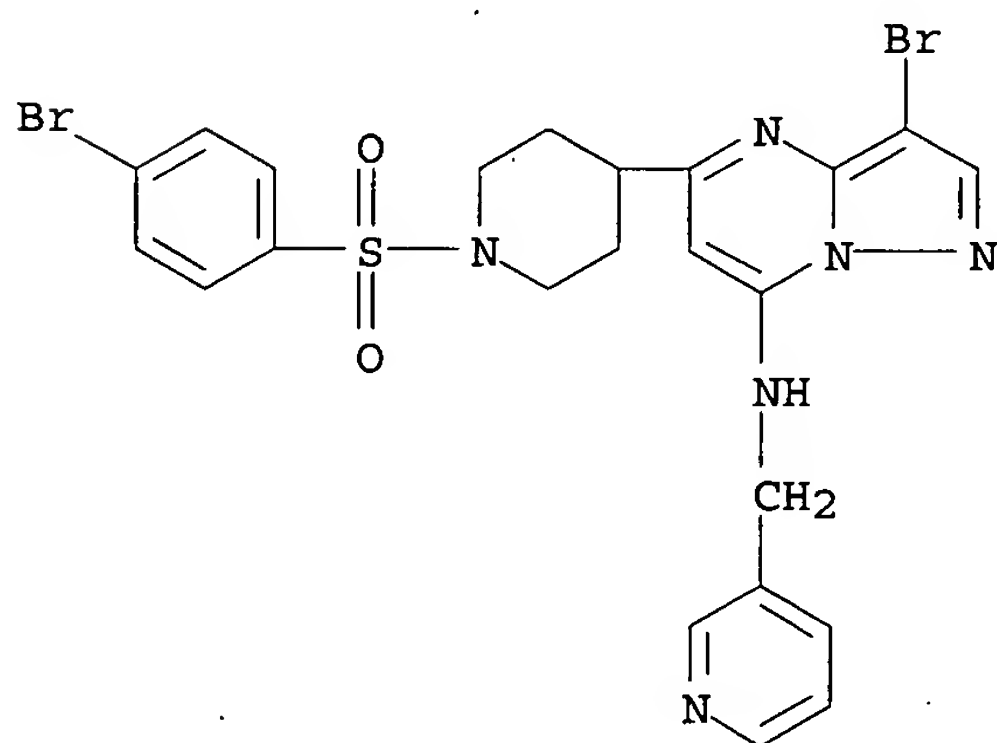
RN 677793-94-1 HCAPLUS  
 CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)





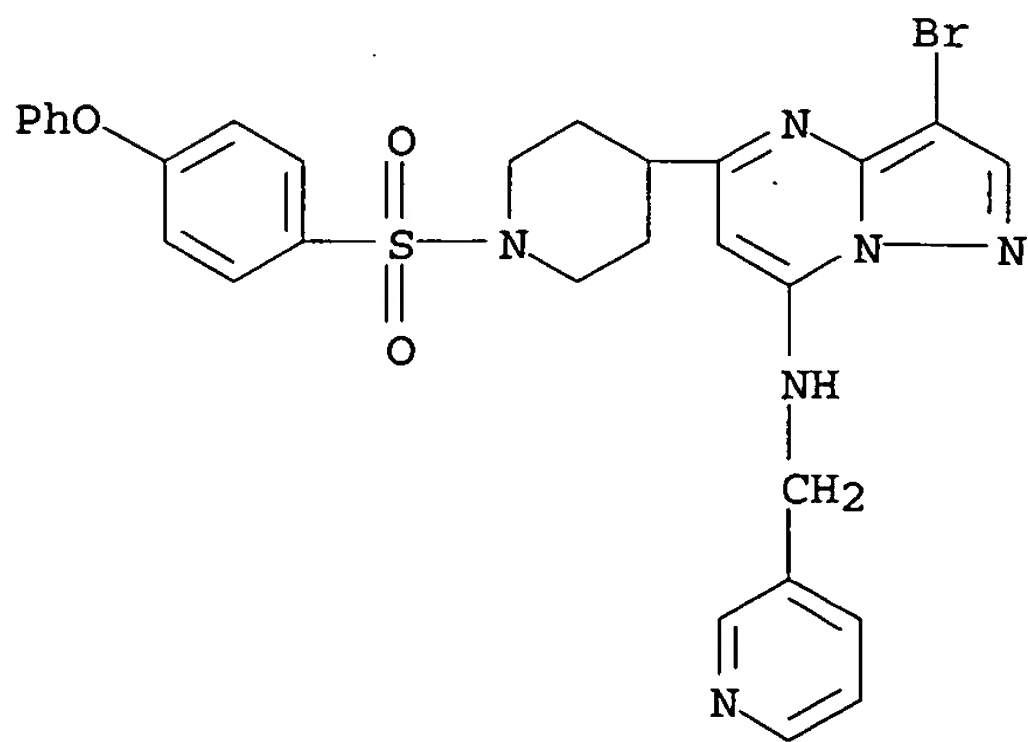
RN 677793-95-2 HCAPLUS

CN Piperidine, 1-[(4-bromophenyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

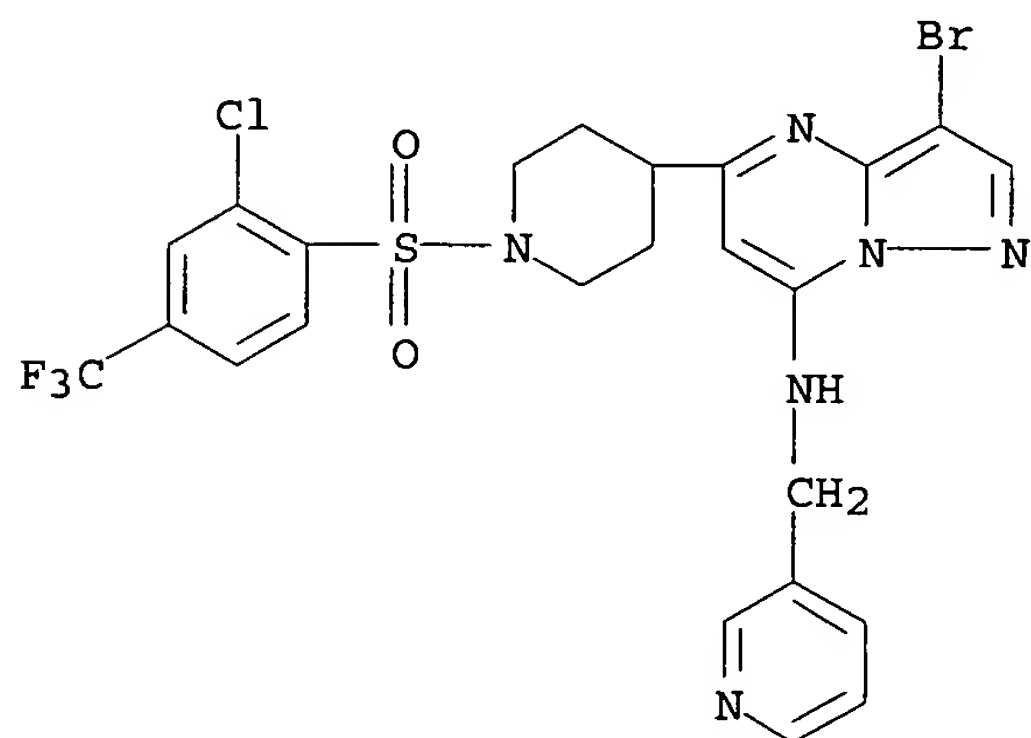


RN 677793-96-3 HCAPLUS

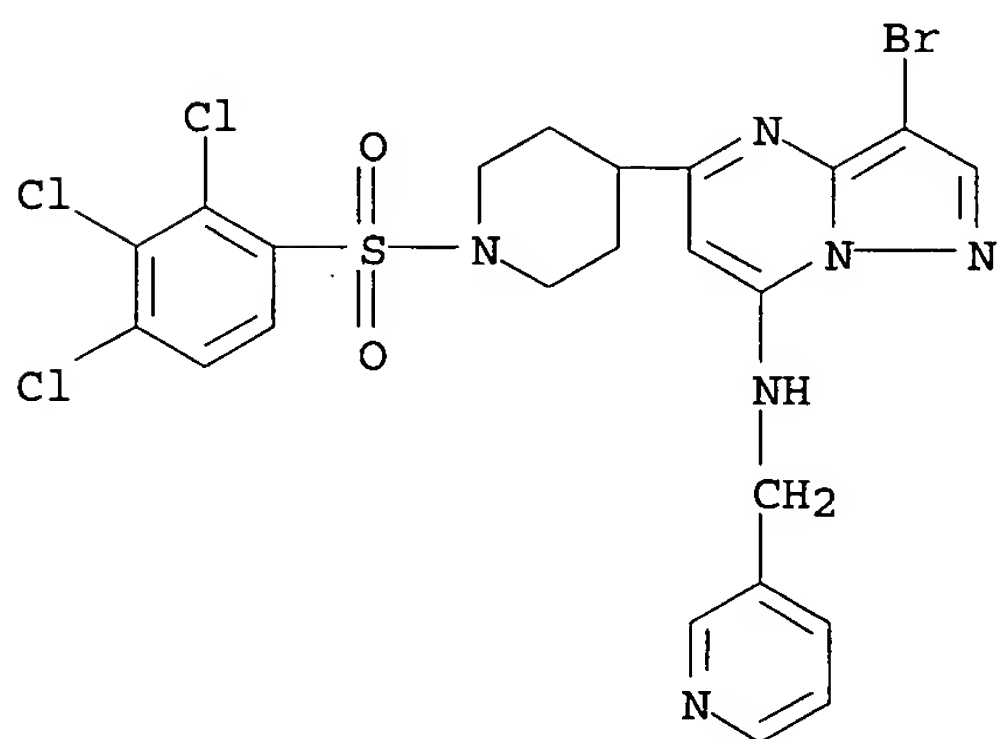
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-phenoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



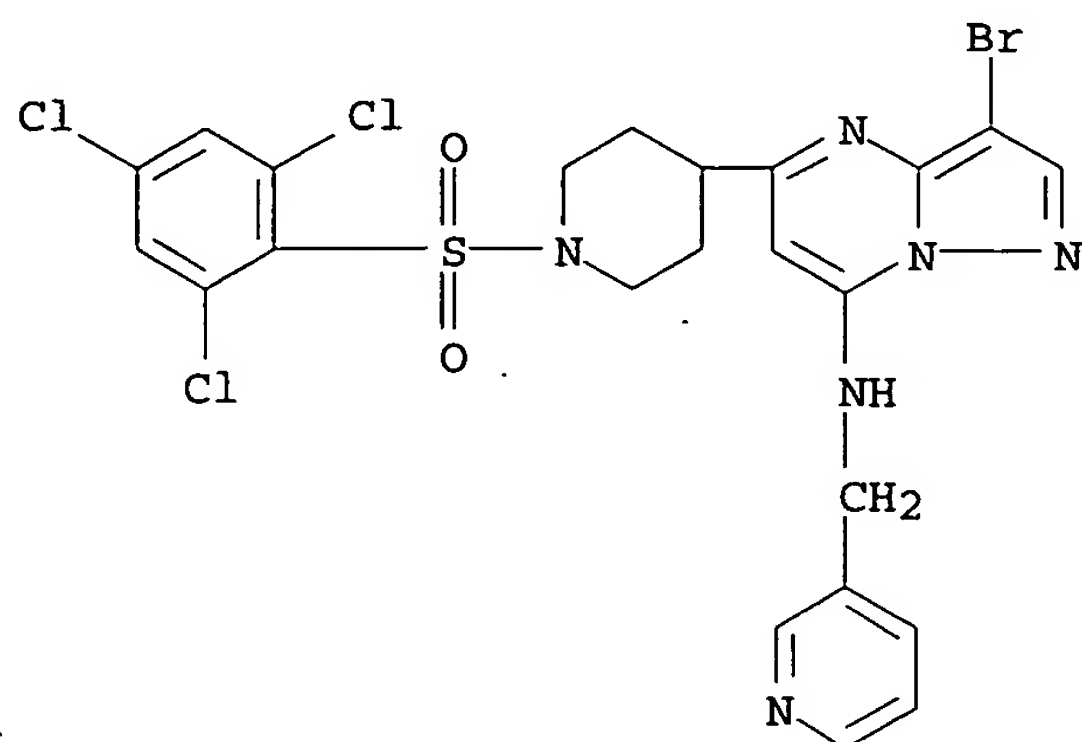
RN 677793-97-4 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl]- (9CI)  
 (CA INDEX NAME)



RN 677793-98-5 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3,4-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

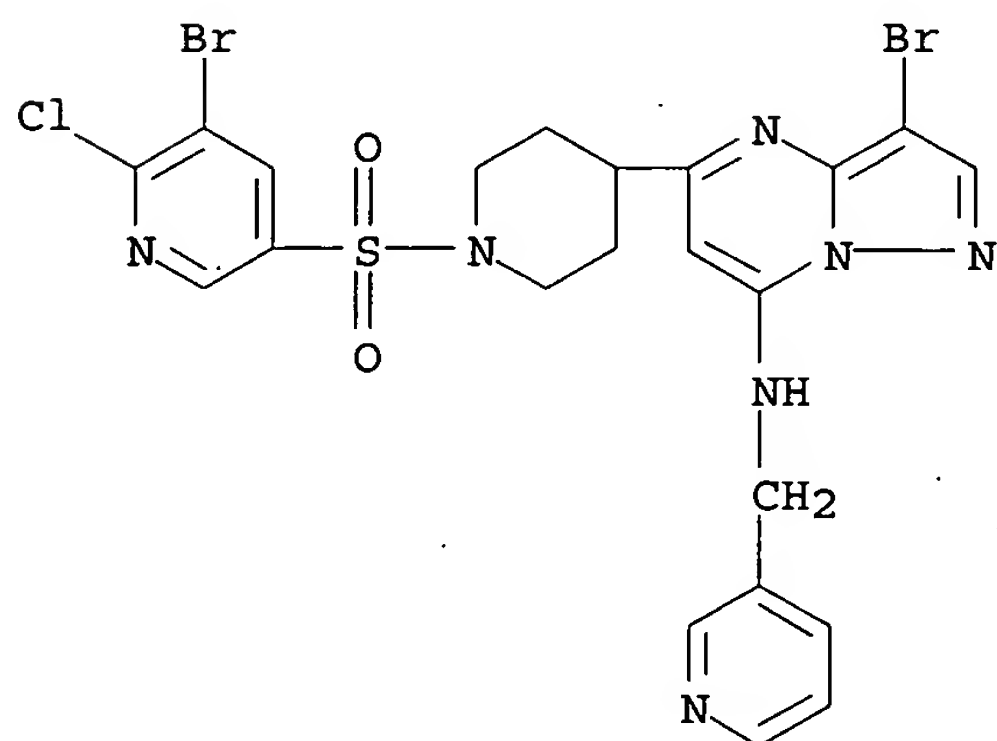


RN 677793-99-6 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



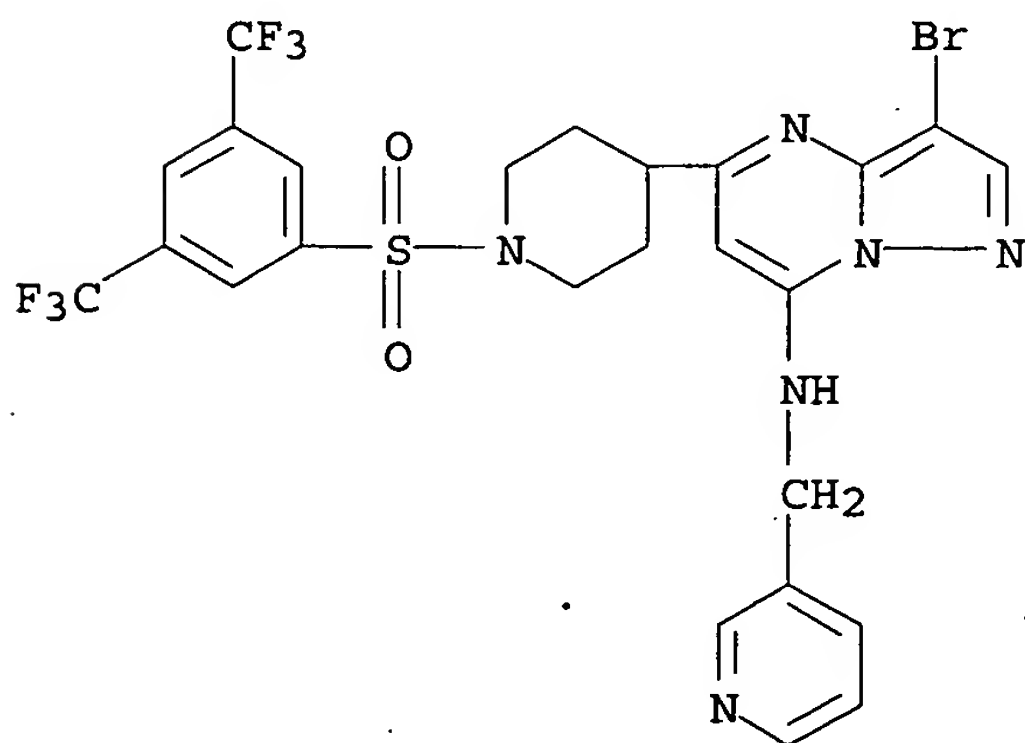
RN 677794-00-2 HCAPLUS

CN Piperidine, 1-[(5-bromo-6-chloro-3-pyridinyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



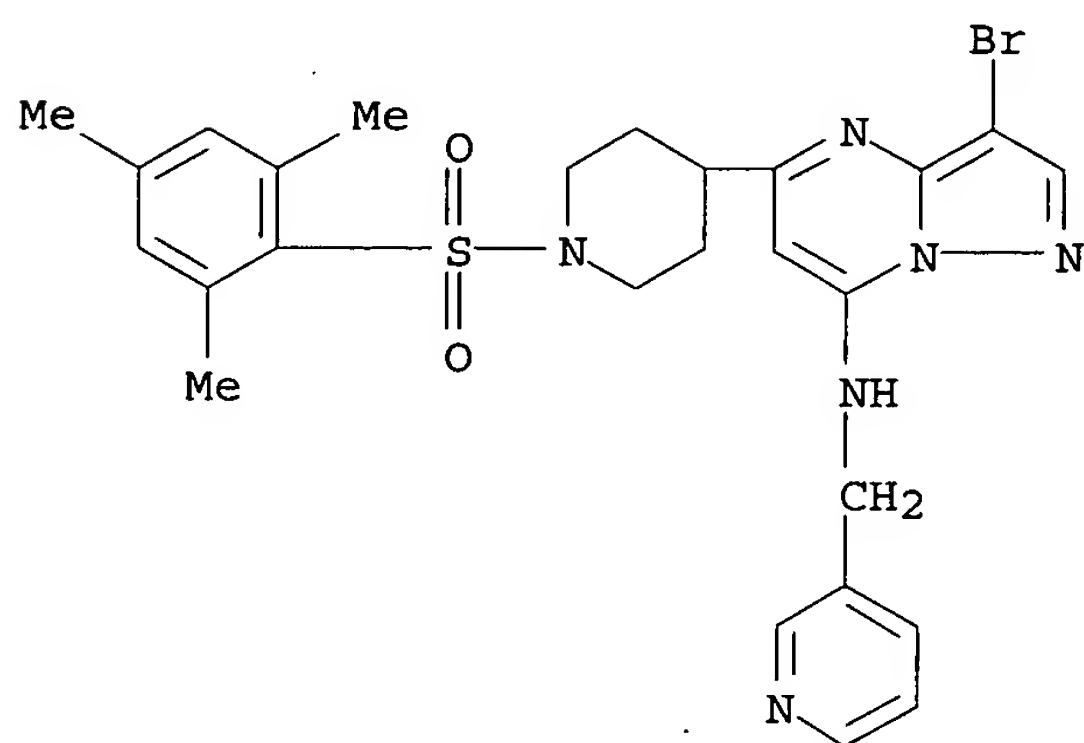
RN 677794-01-3 HCAPLUS

CN Piperidine, 1-[[3,5-bis(trifluoromethyl)phenyl]sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



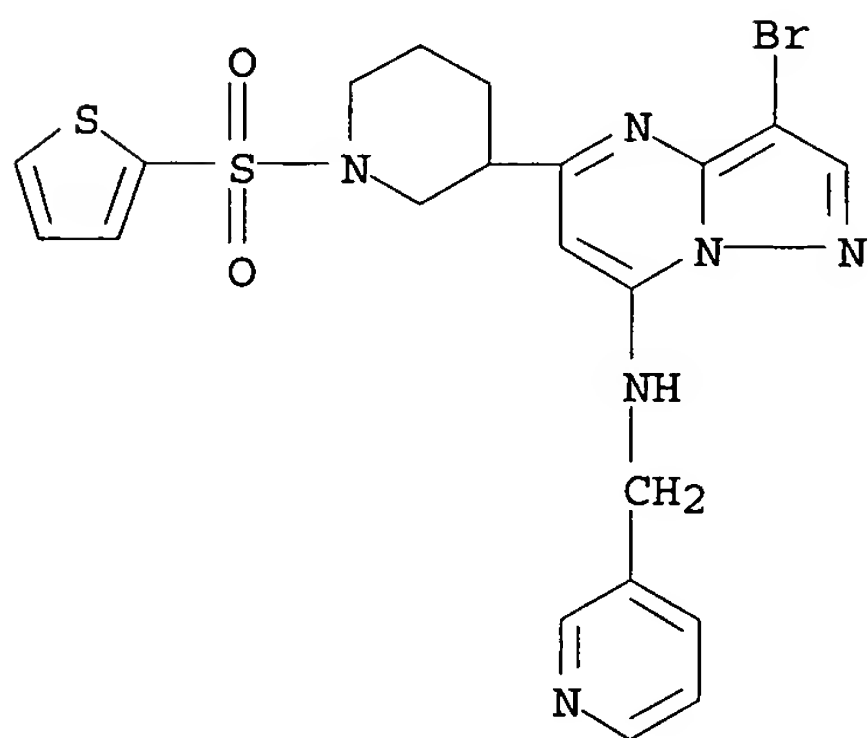
RN 677794-02-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



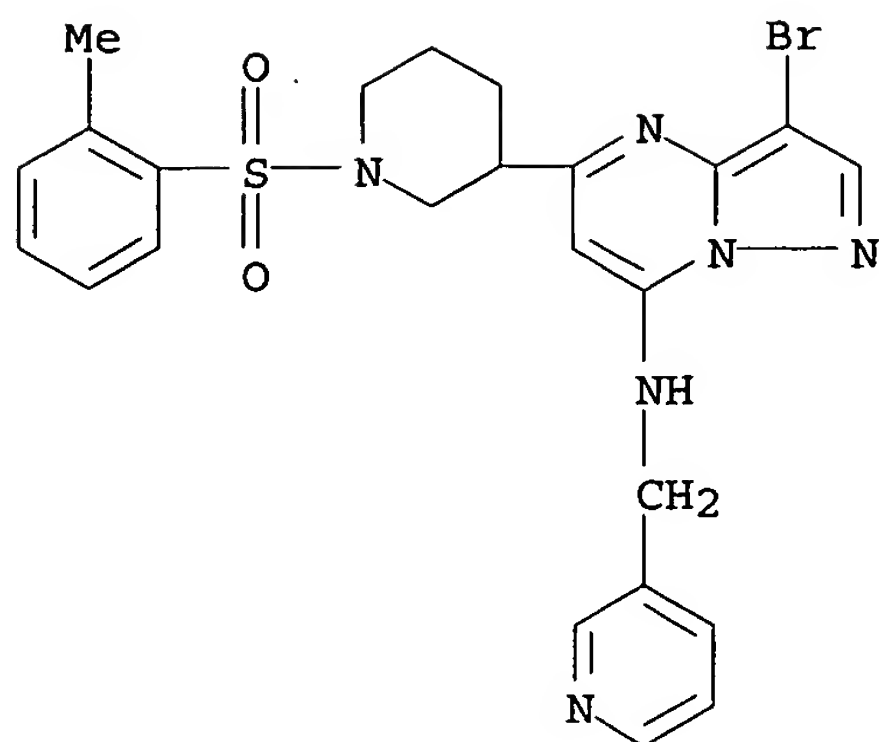
RN 677794-03-5 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)



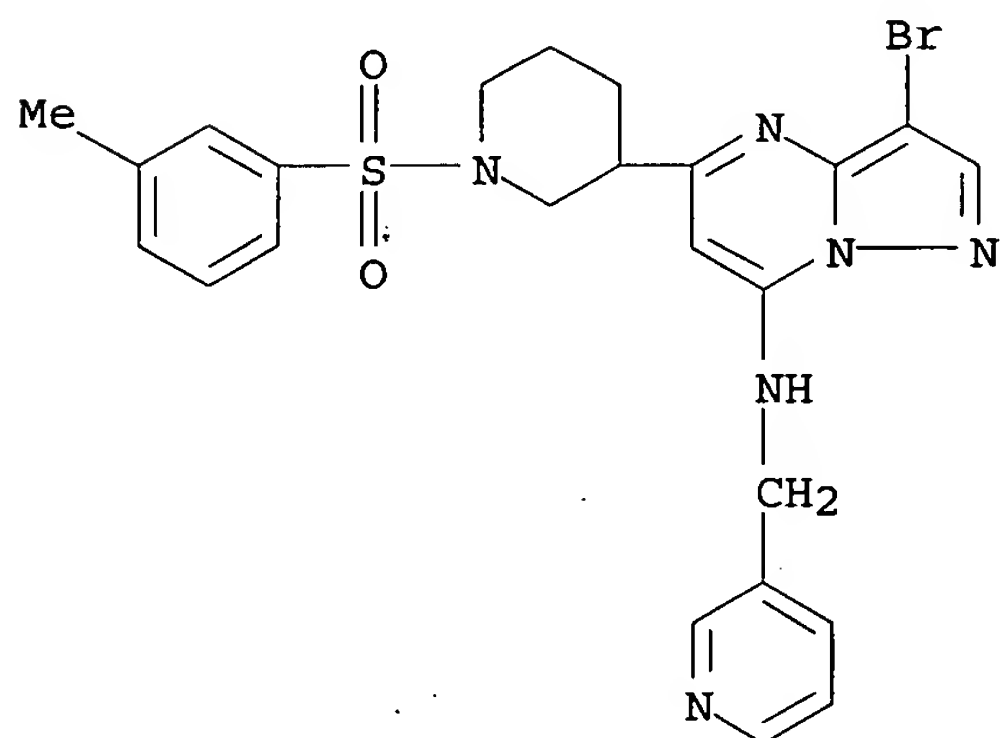
RN 677794-04-6 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



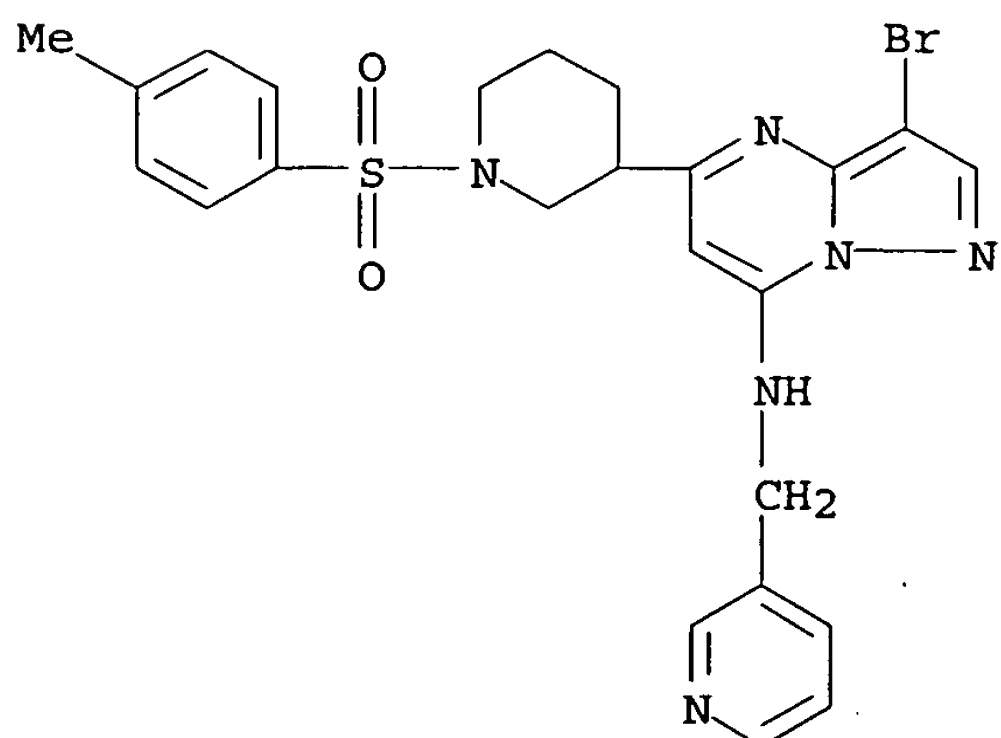
RN 677794-05-7 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



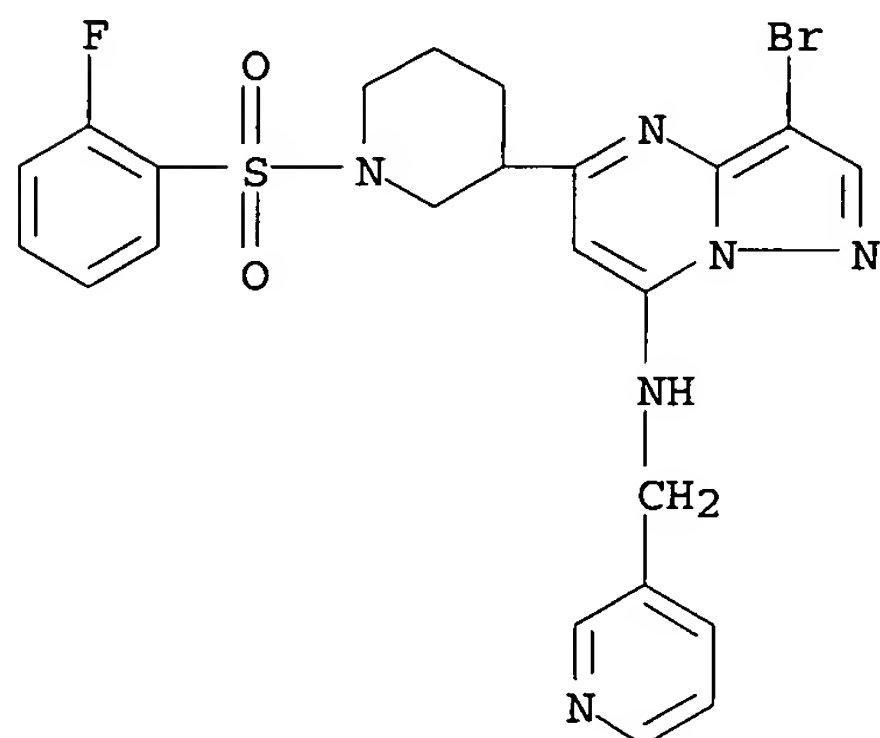
RN 677794-06-8 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



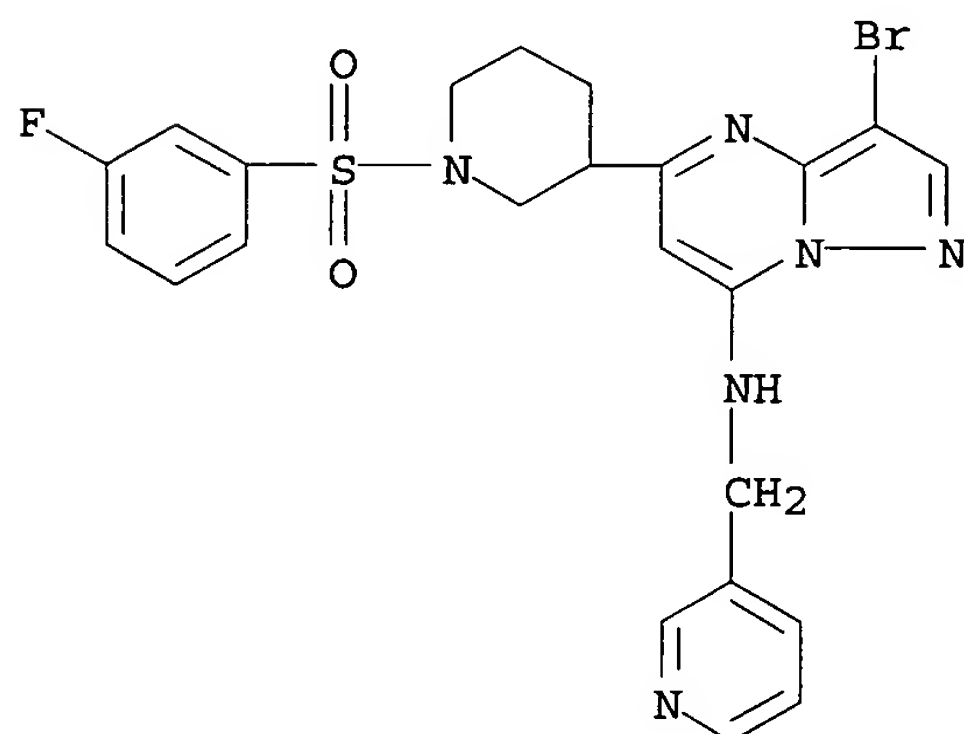
RN 677794-07-9 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



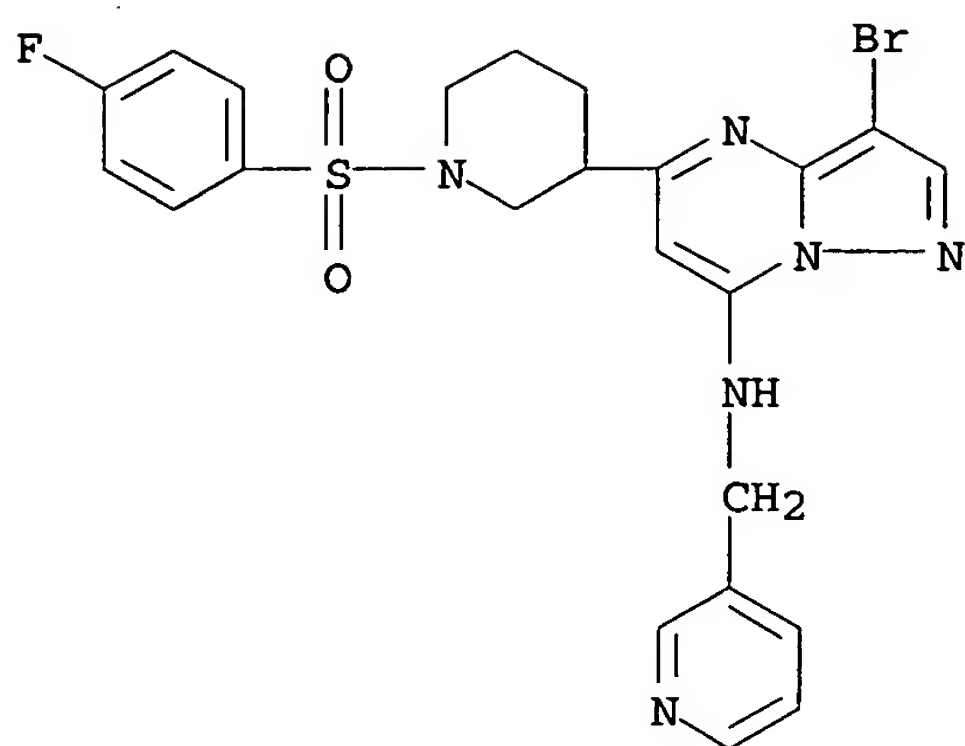
RN 677794-08-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



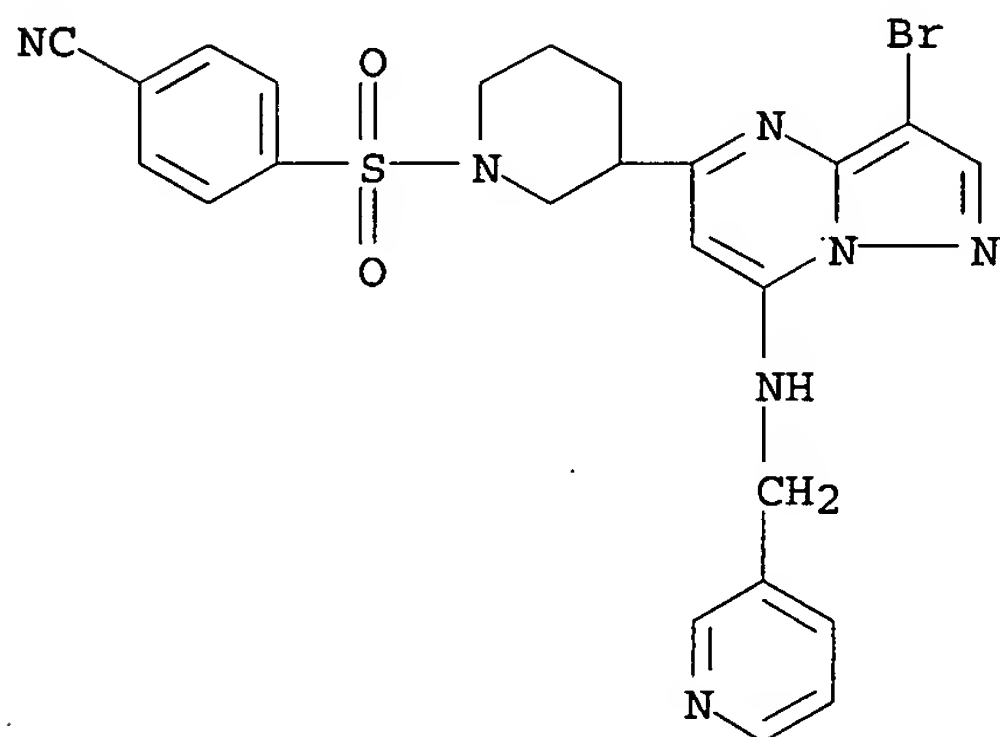
RN 677794-09-1 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



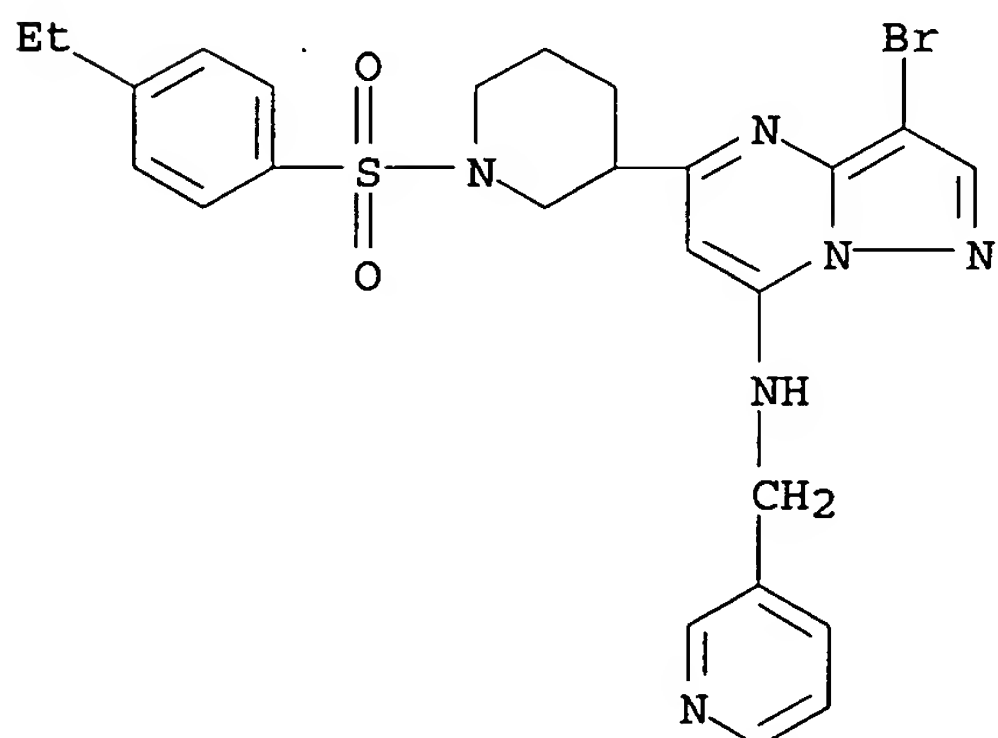
RN 677794-10-4 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



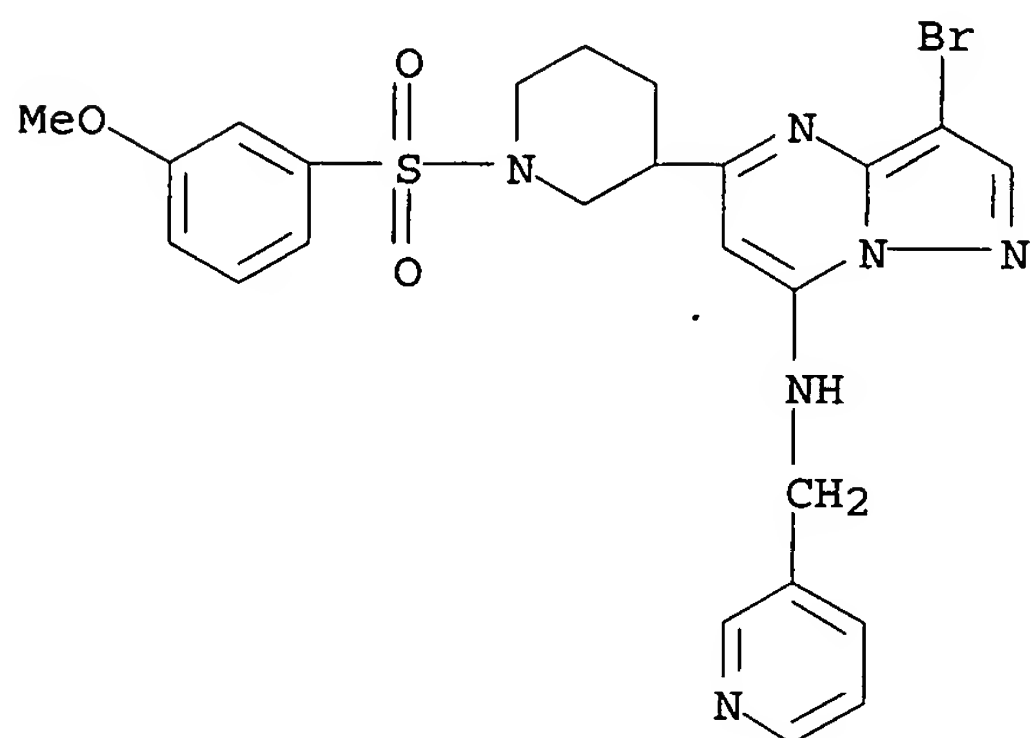
RN 677794-12-6 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-ethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



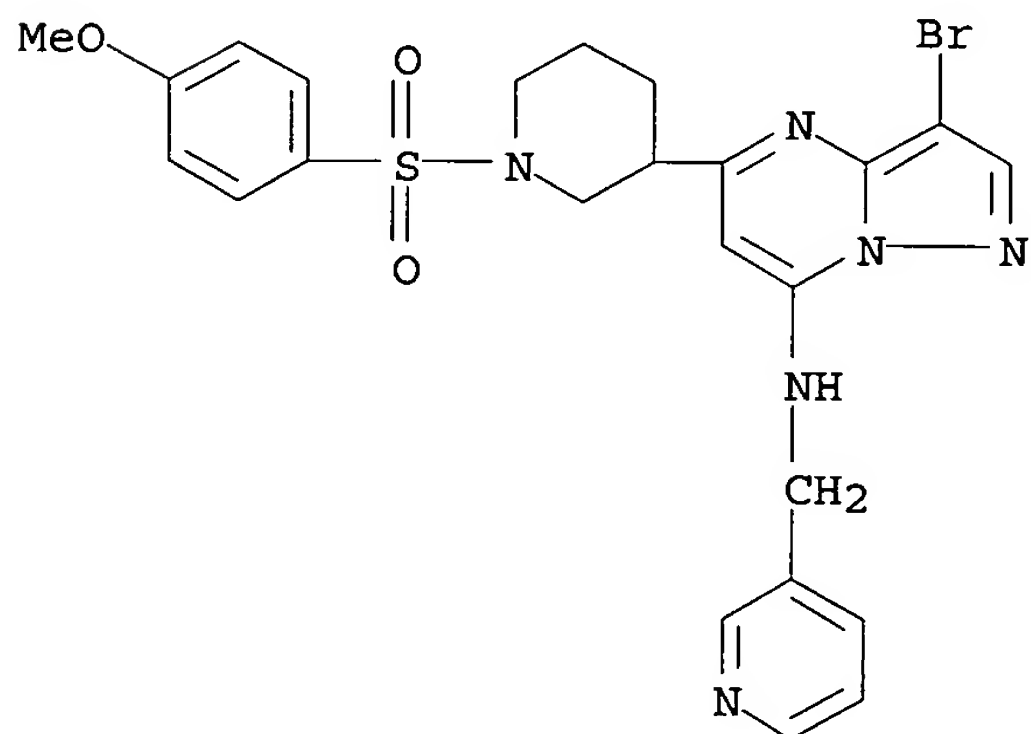
RN 677794-13-7 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-14-8 HCAPLUS

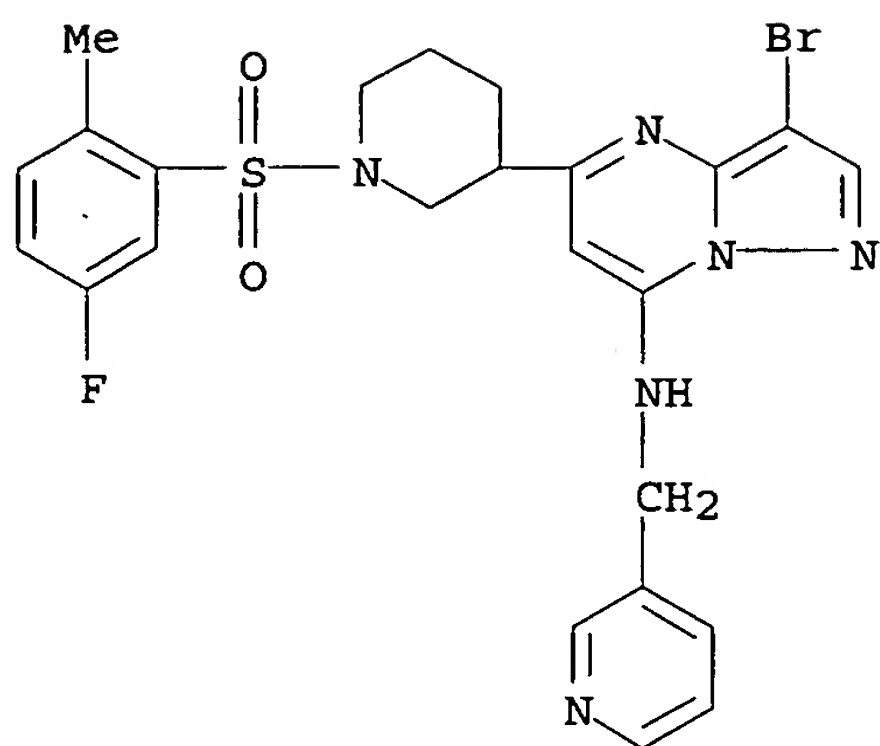
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-15-9 HCAPLUS

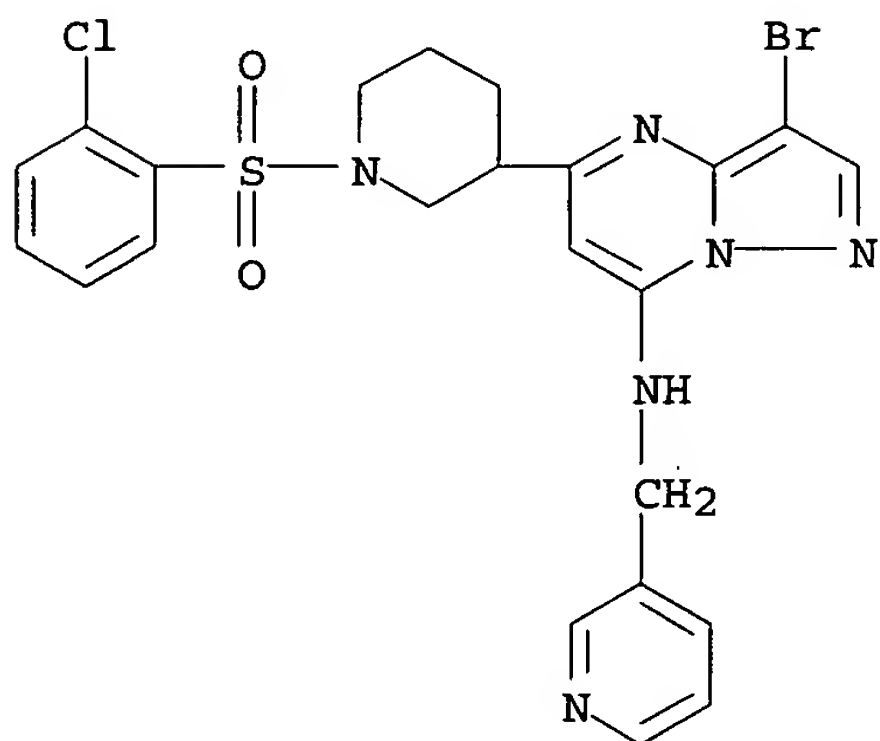
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-fluoro-2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)





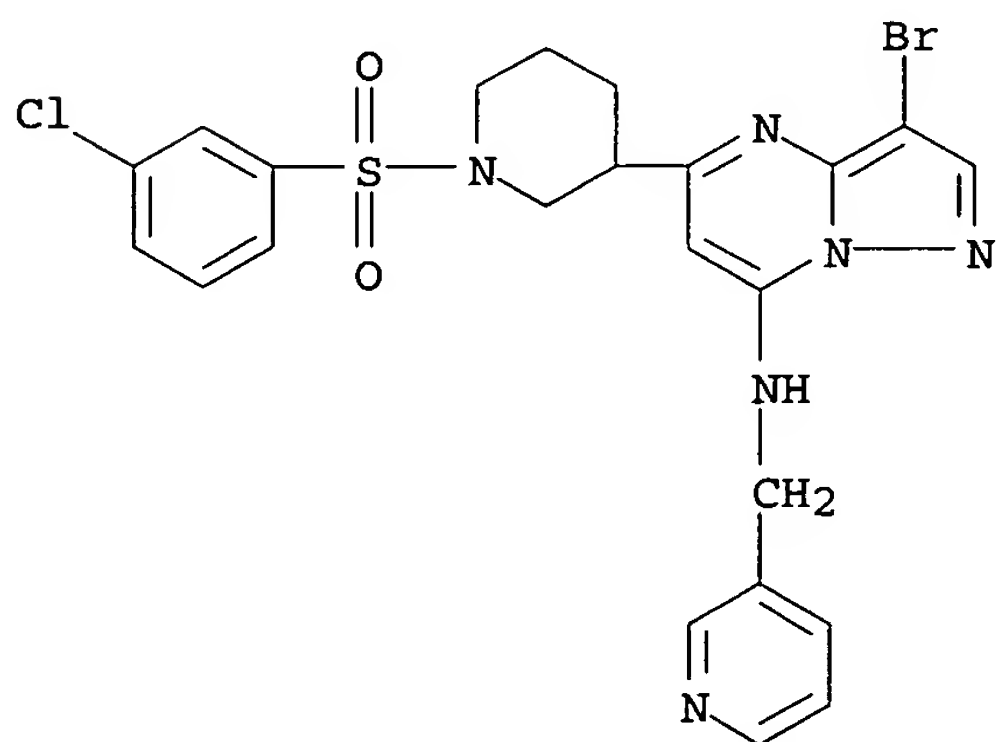
RN 677794-16-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



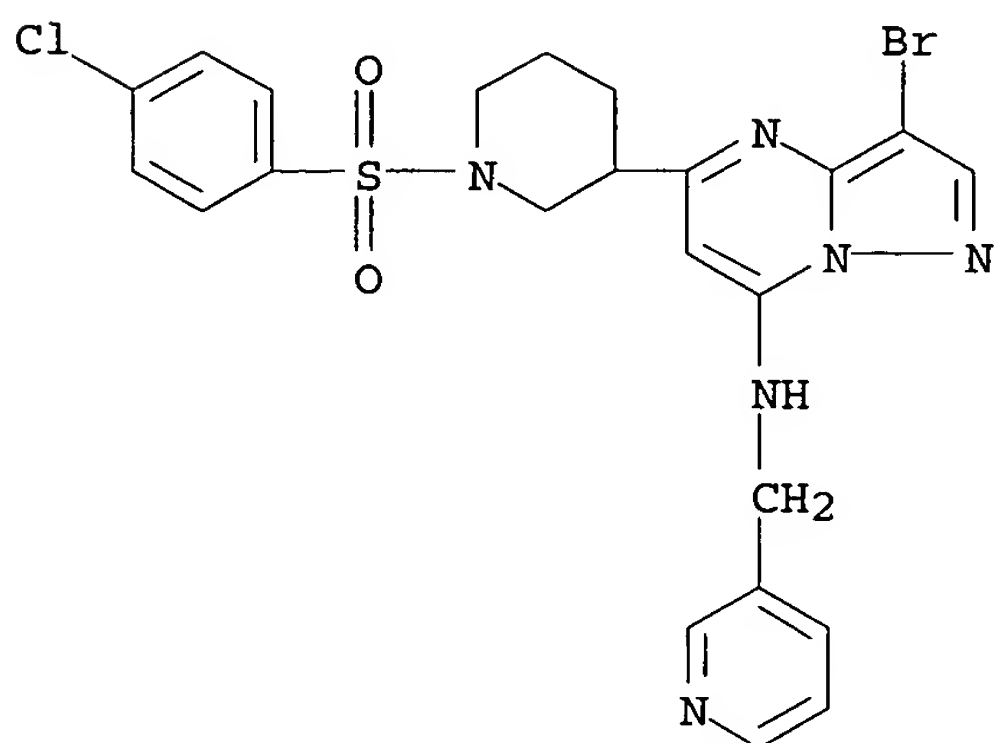
RN 677794-17-1 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



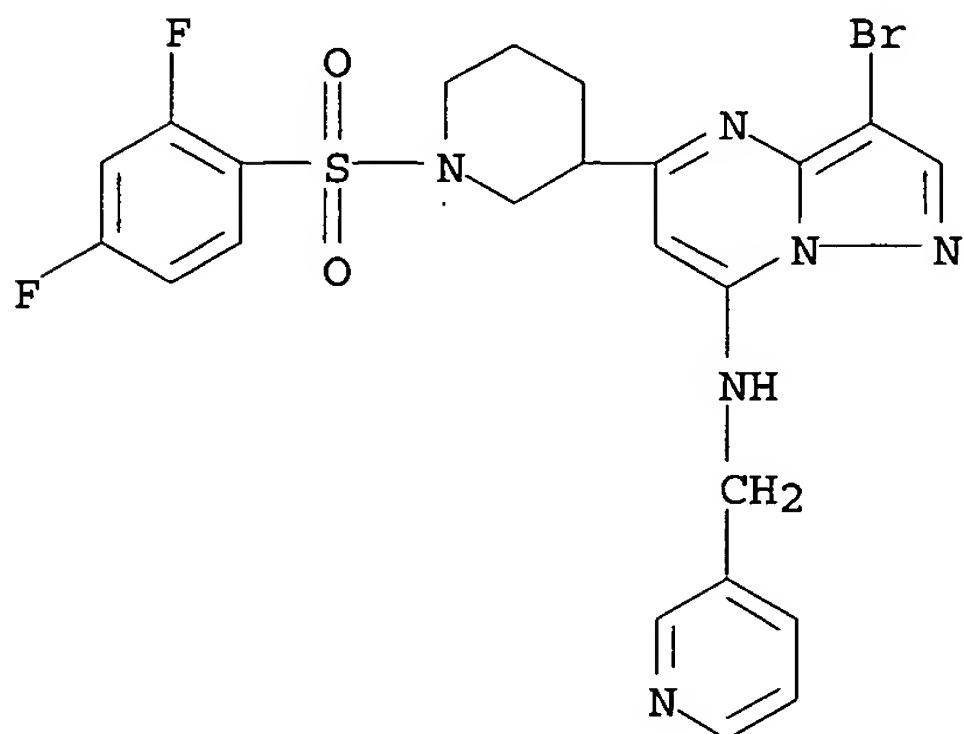
RN 677794-18-2 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-19-3 HCAPLUS

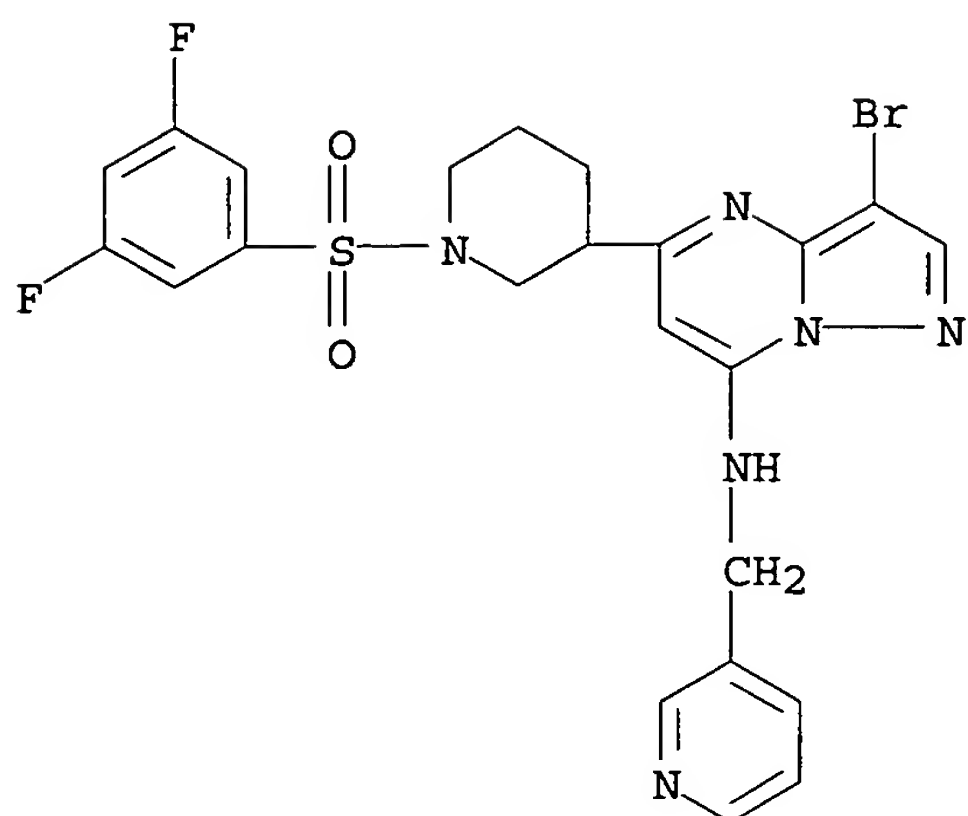
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-20-6 HCAPLUS

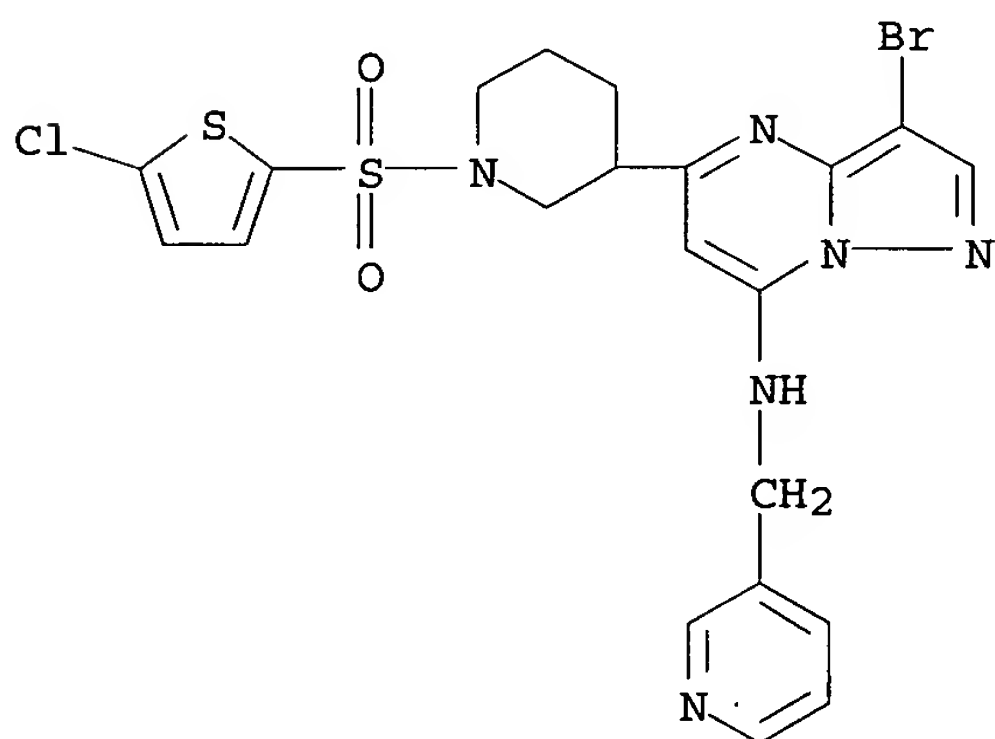
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)





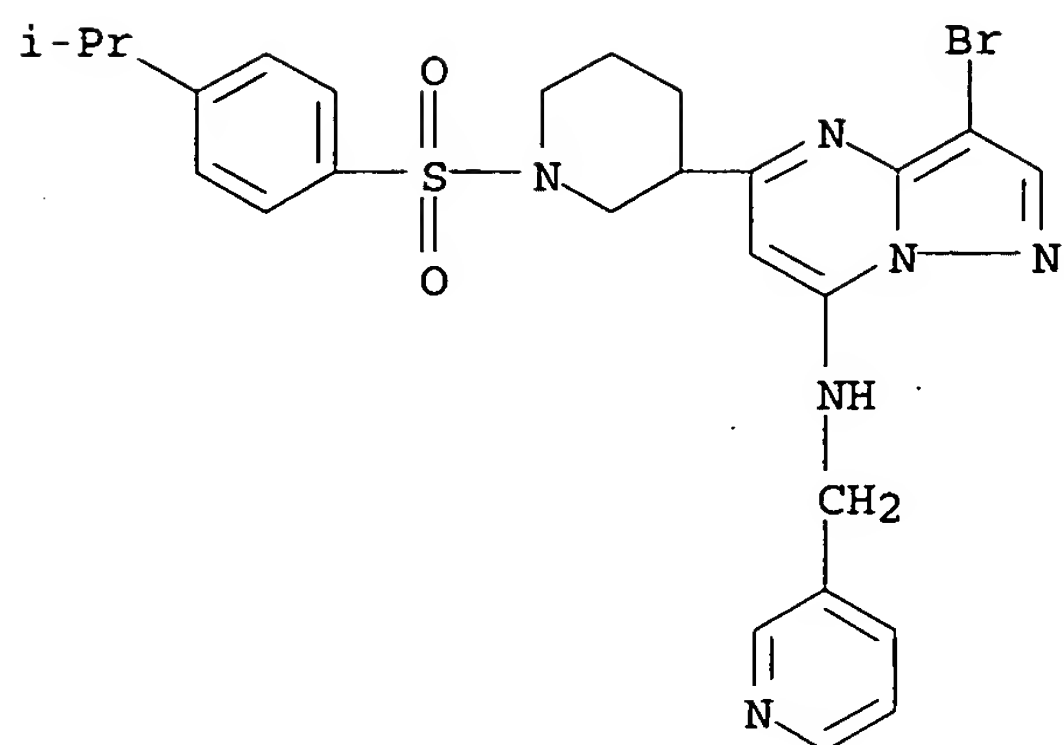
RN 677794-23-9 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-2-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)



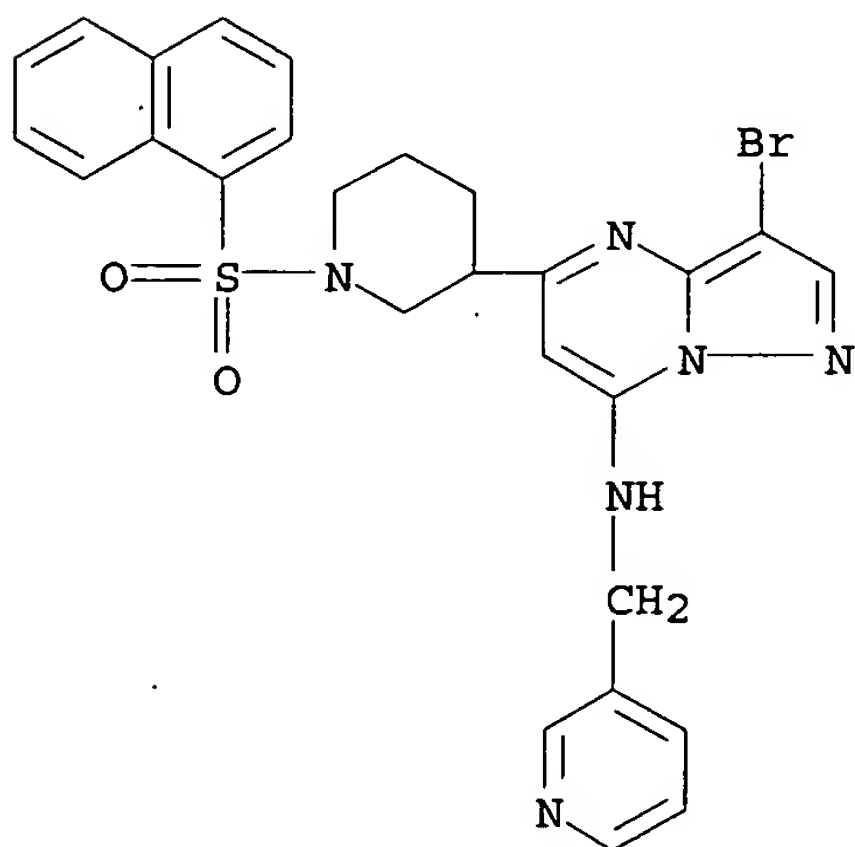
RN 677794-24-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1-methylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



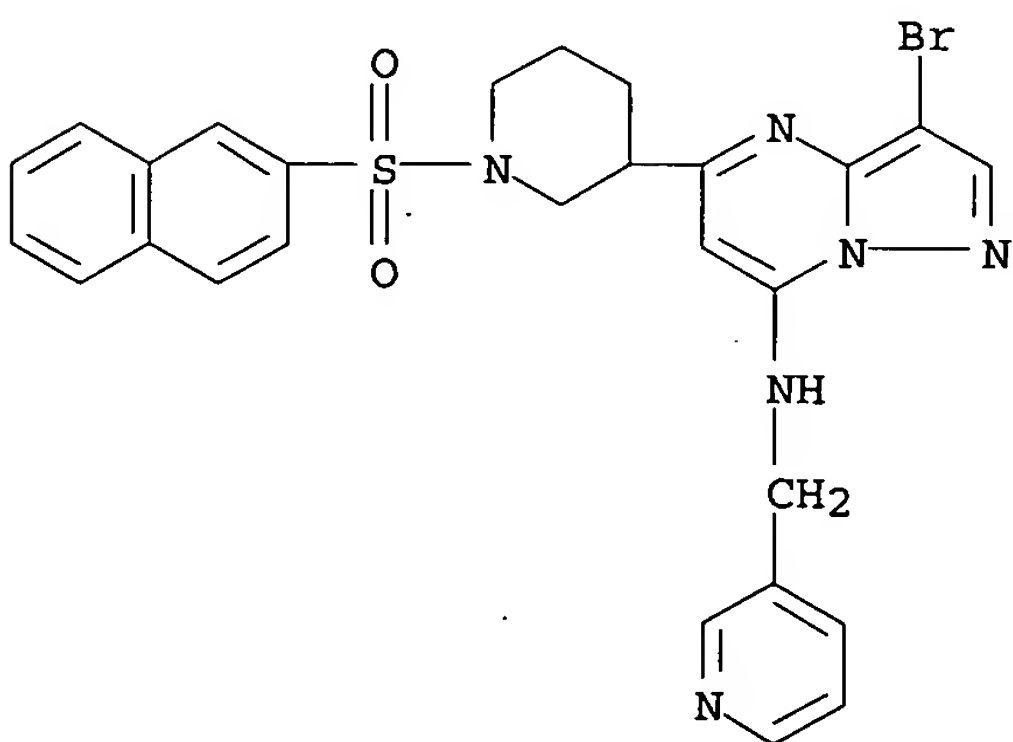
RN 677794-25-1 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

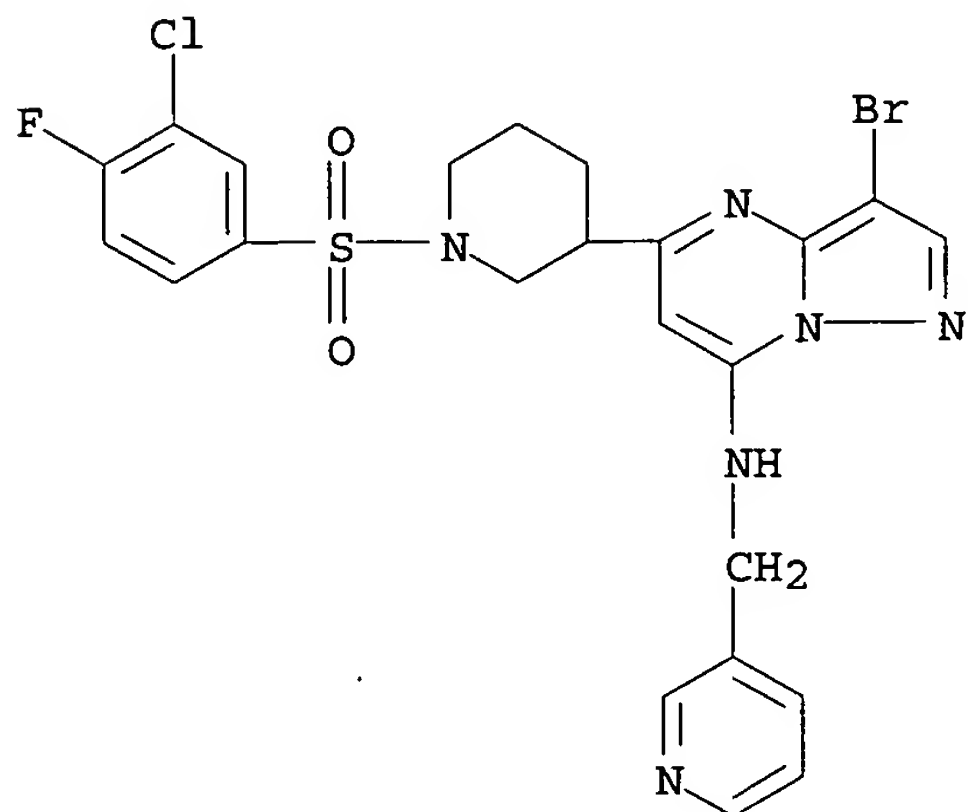


RN 677794-26-2 HCAPLUS

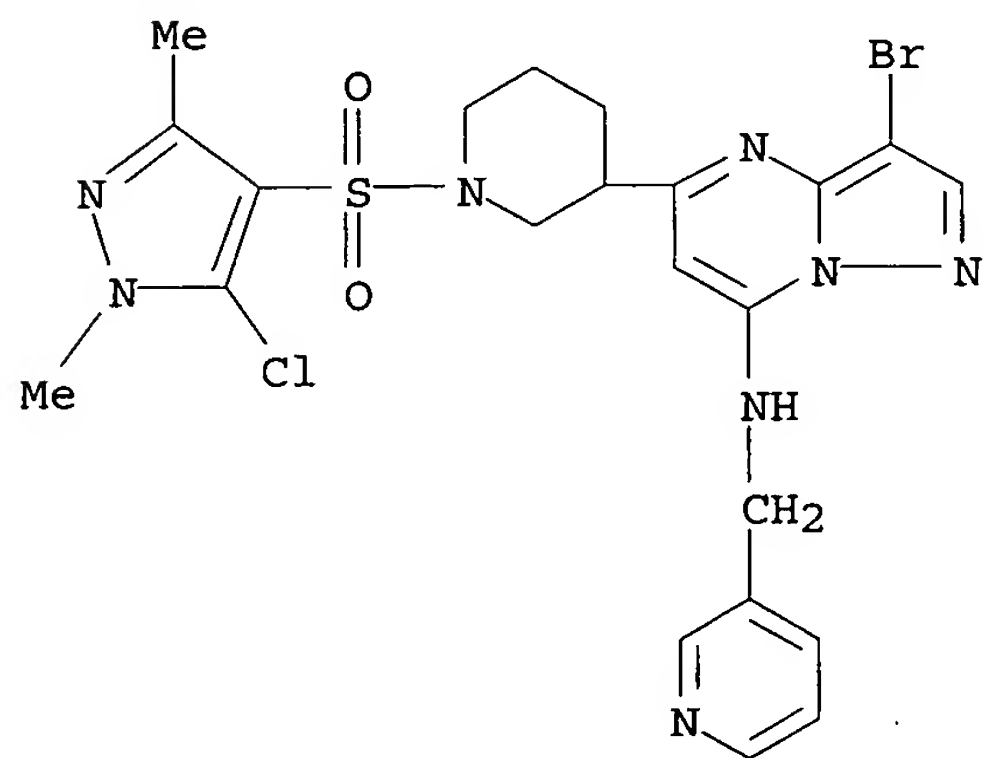
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



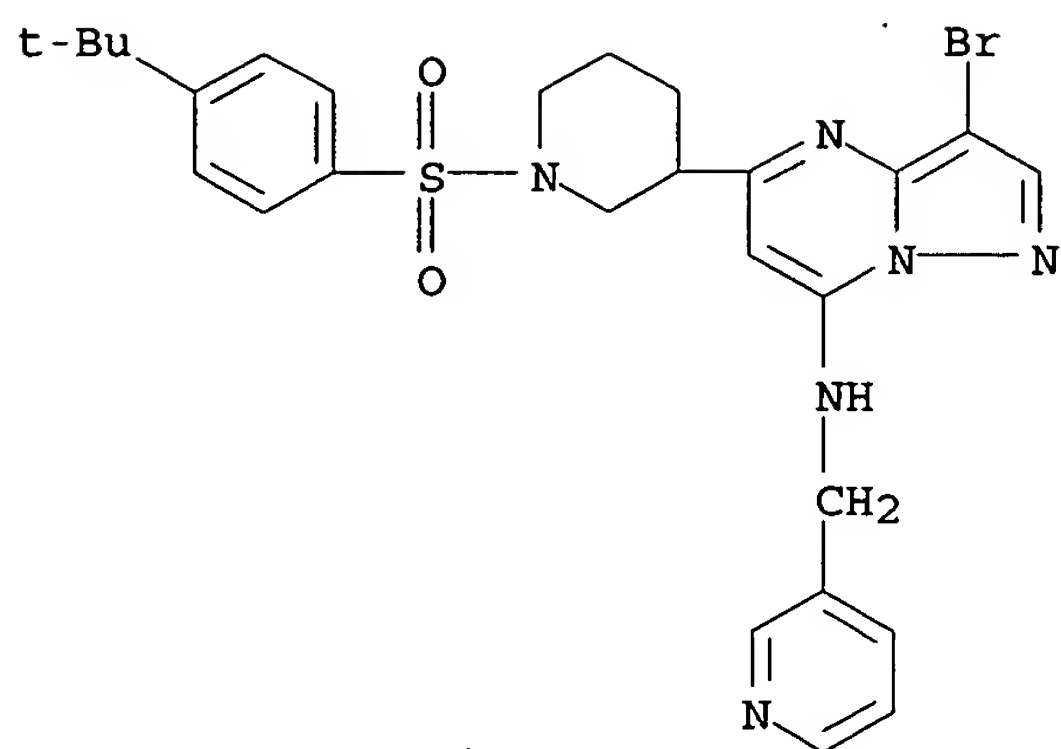
RN 677794-27-3 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



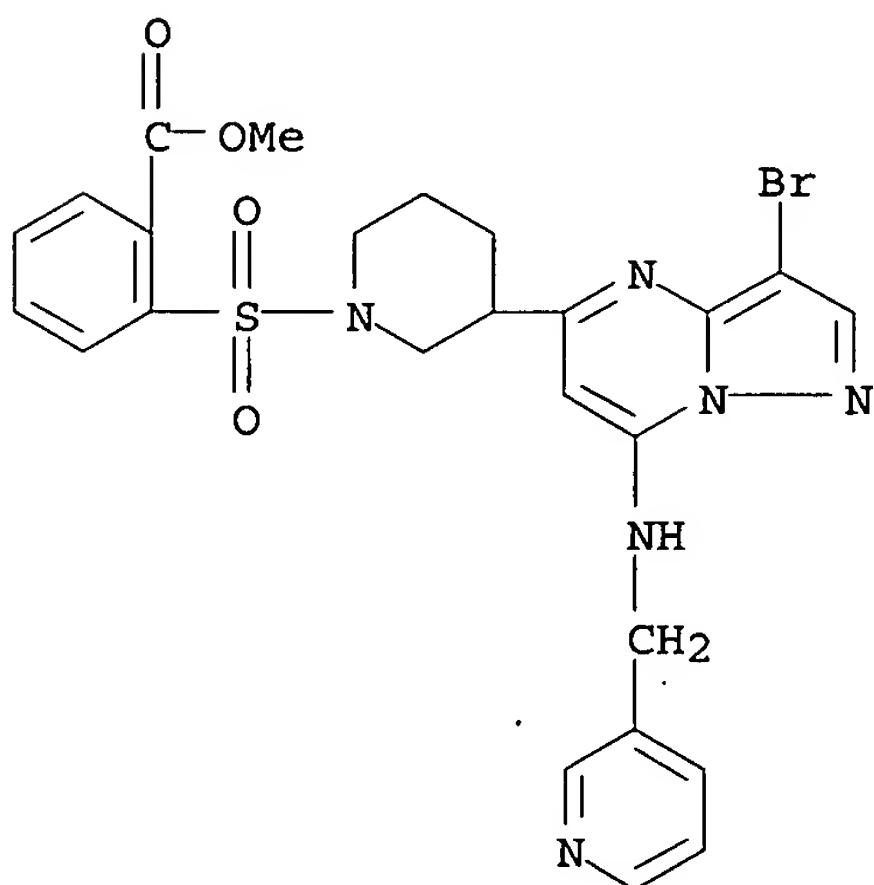
RN 677794-28-4 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)



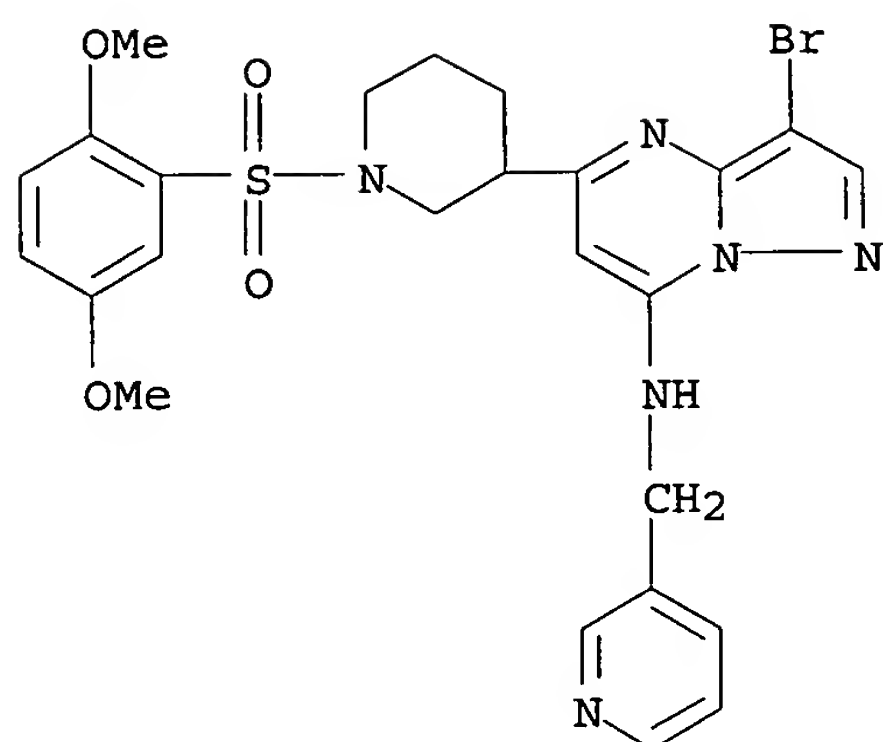
RN 677794-29-5 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



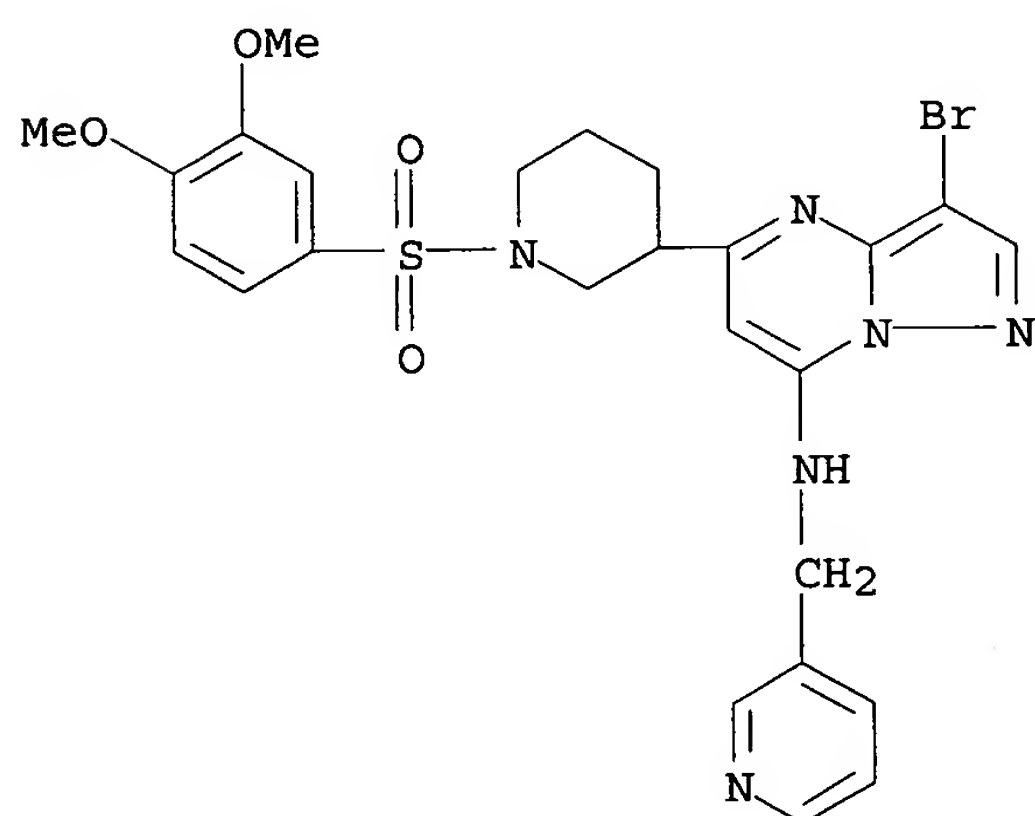
RN 677794-30-8 HCAPLUS  
 CN Benzoic acid, 2-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 677794-31-9 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

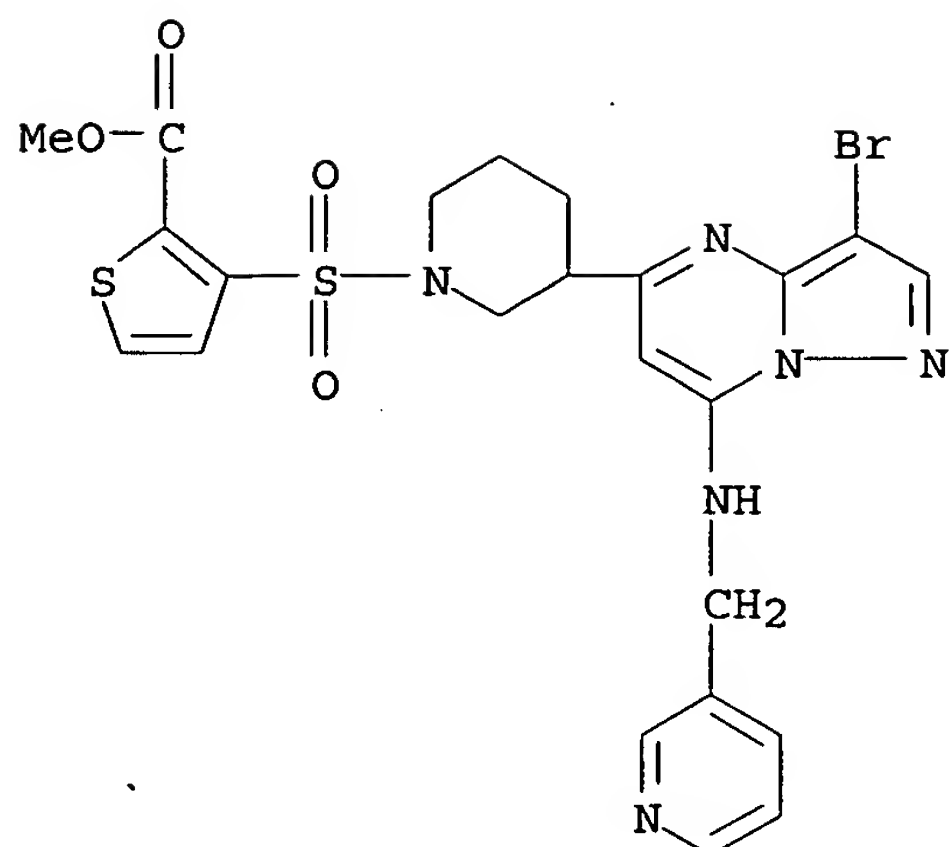


RN 677794-32-0 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

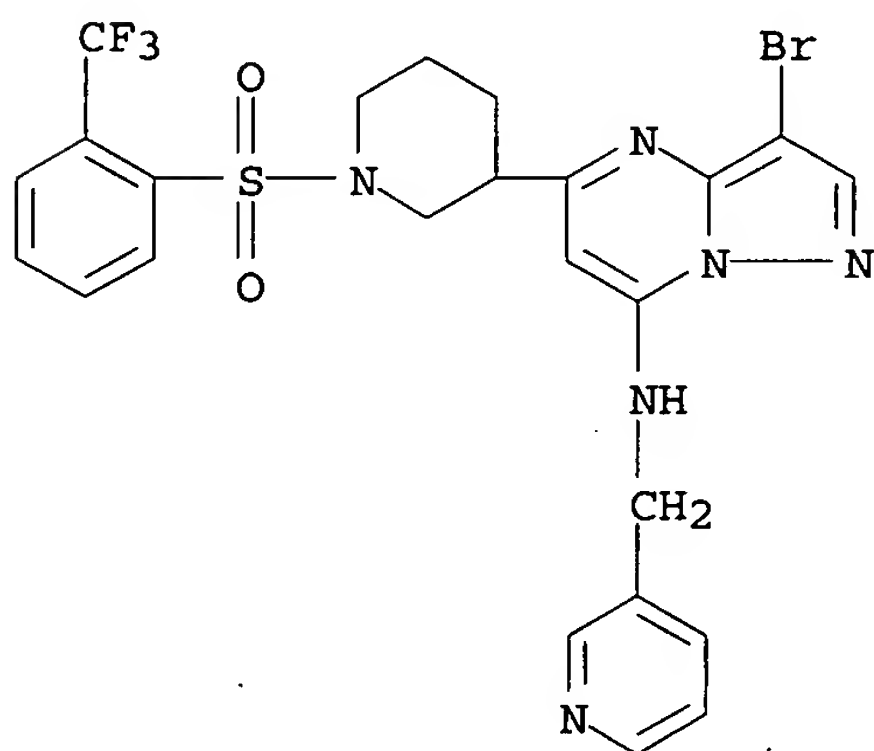


RN 677794-33-1 HCAPLUS  
 CN 2-Thiophenecarboxylic acid, 3-[[[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

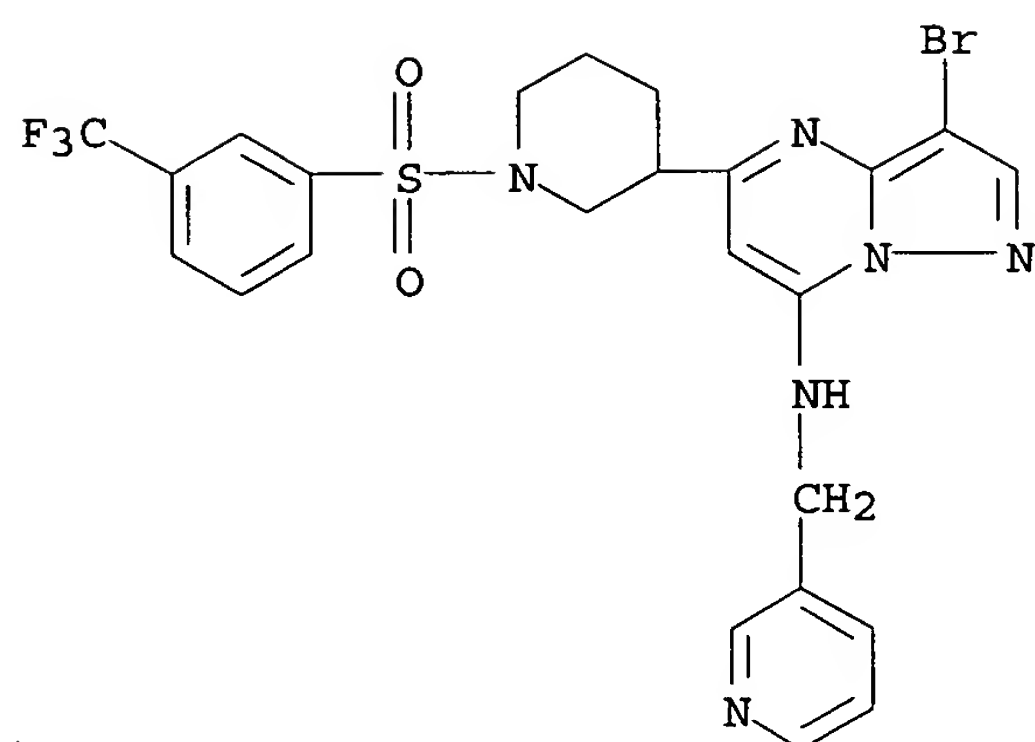




RN 677794-34-2 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

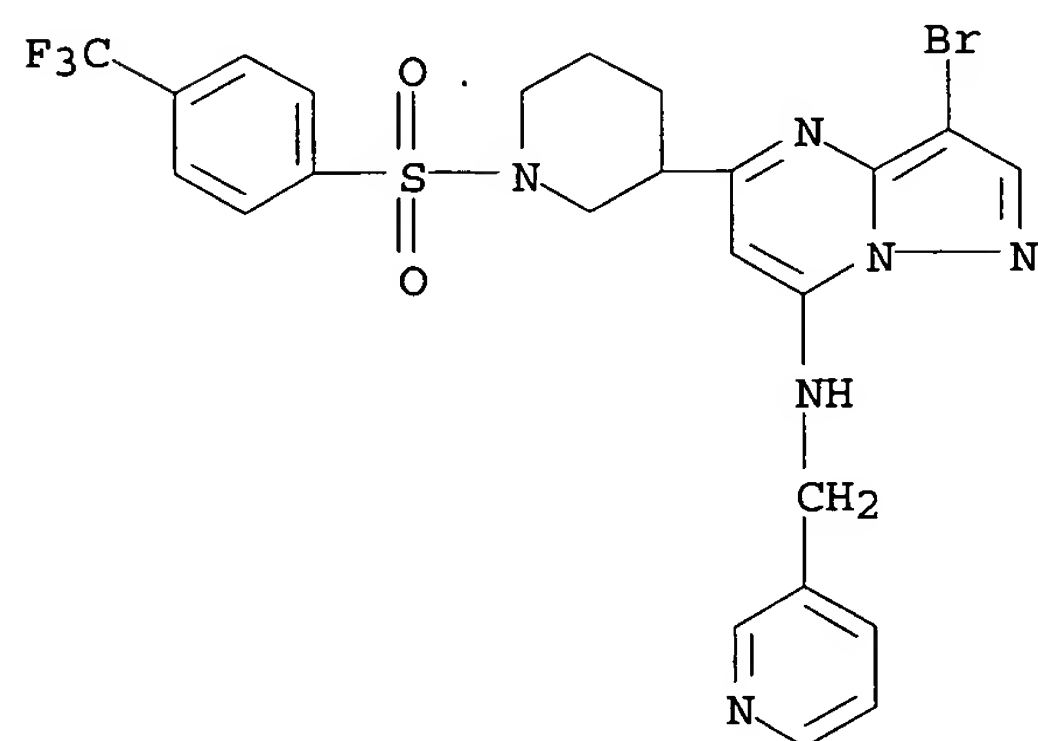


RN 677794-35-3 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



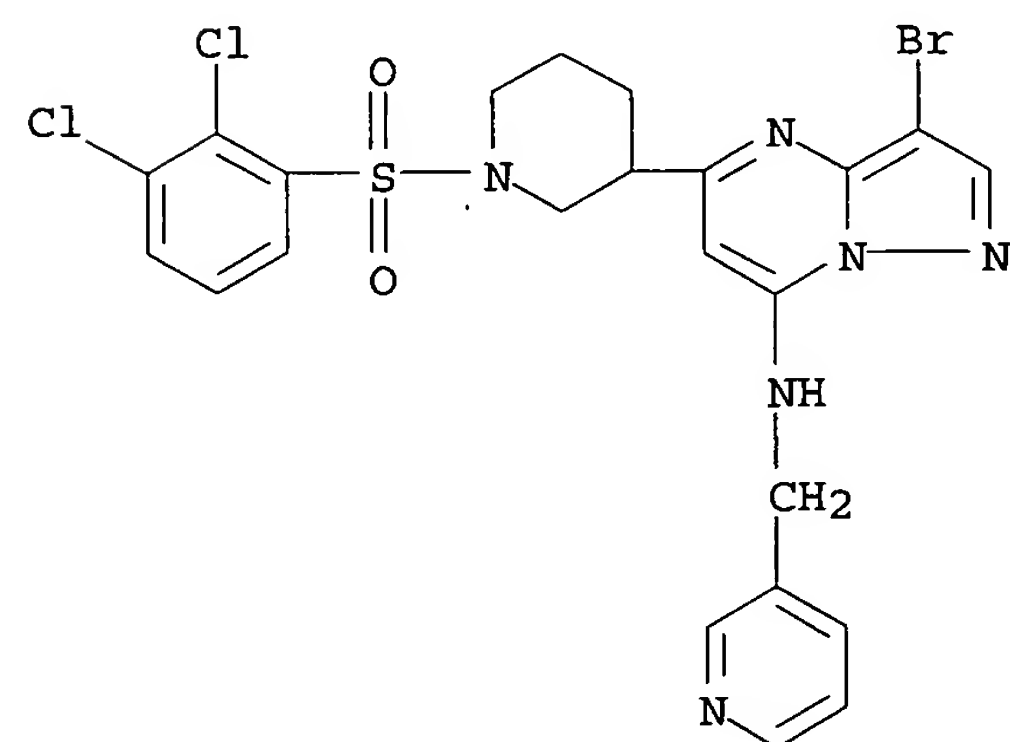
RN 677794-36-4 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

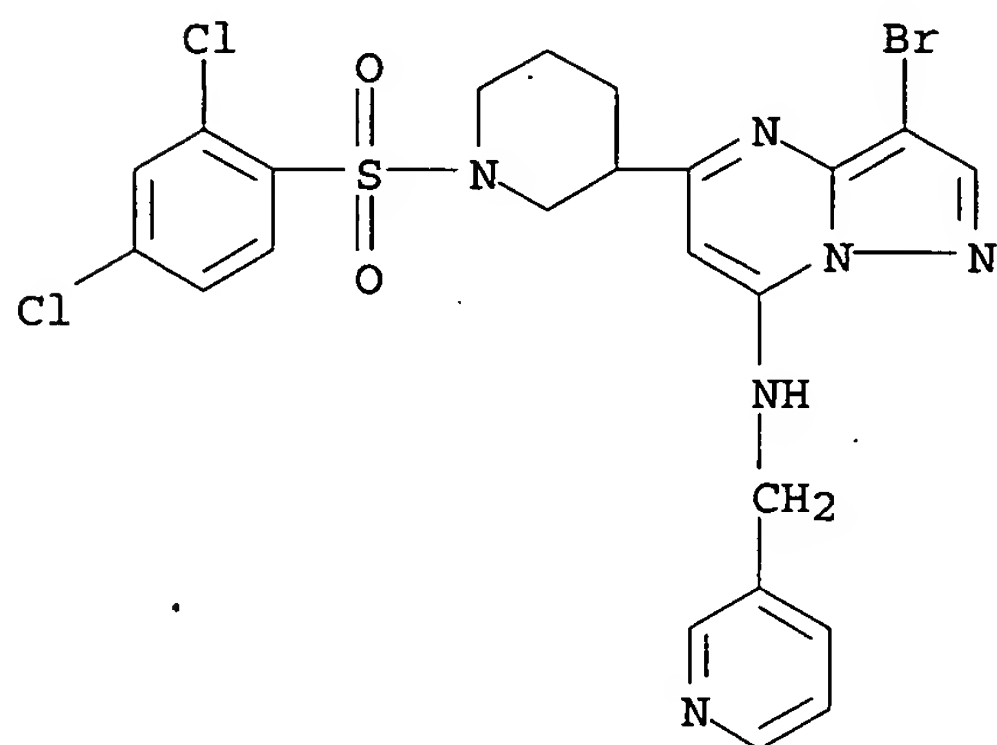


RN 677794-37-5 HCAPLUS

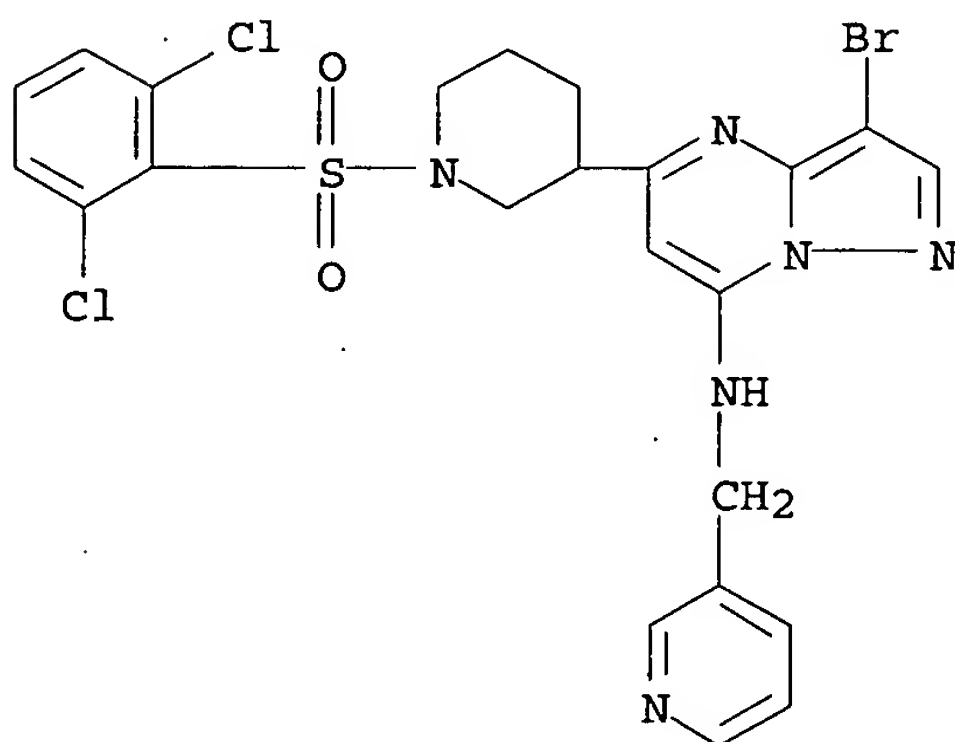
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



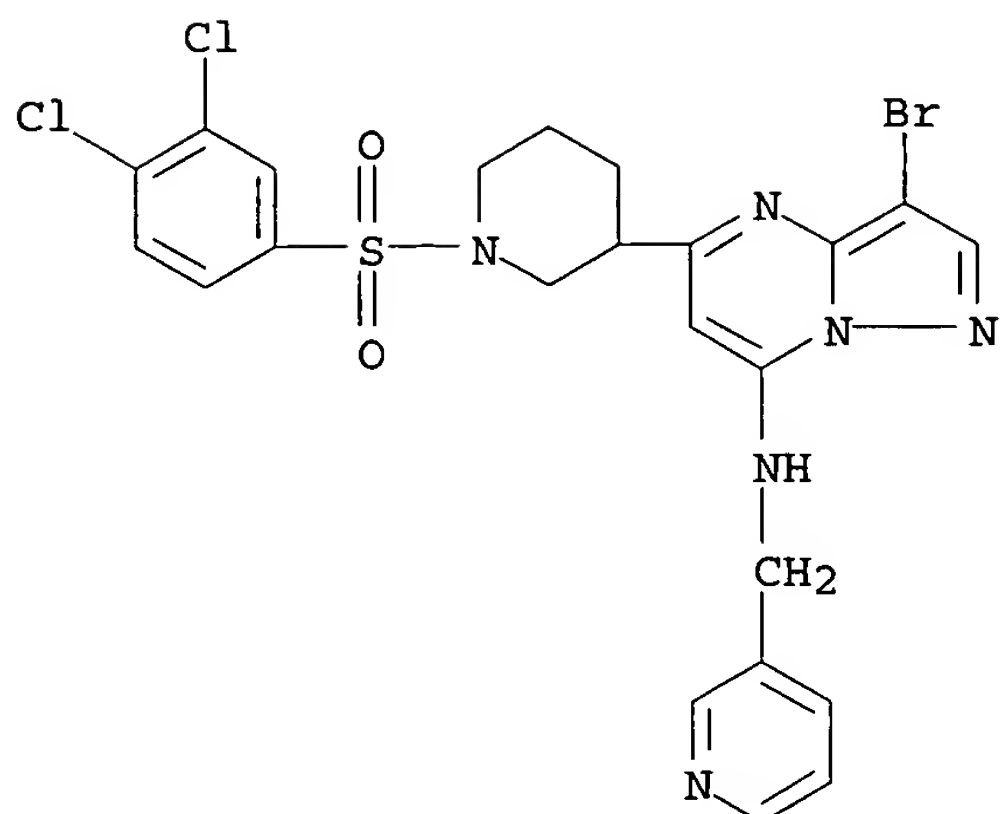
RN 677794-38-6 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-39-7 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

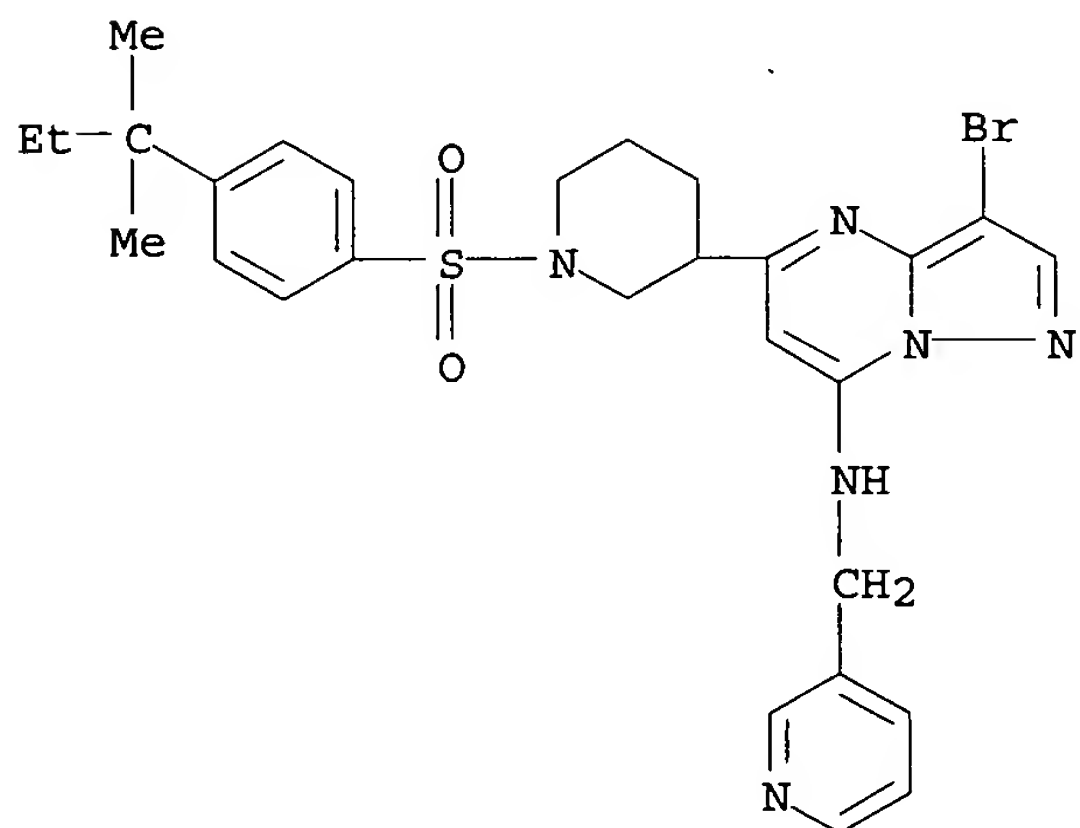


RN 677794-40-0 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



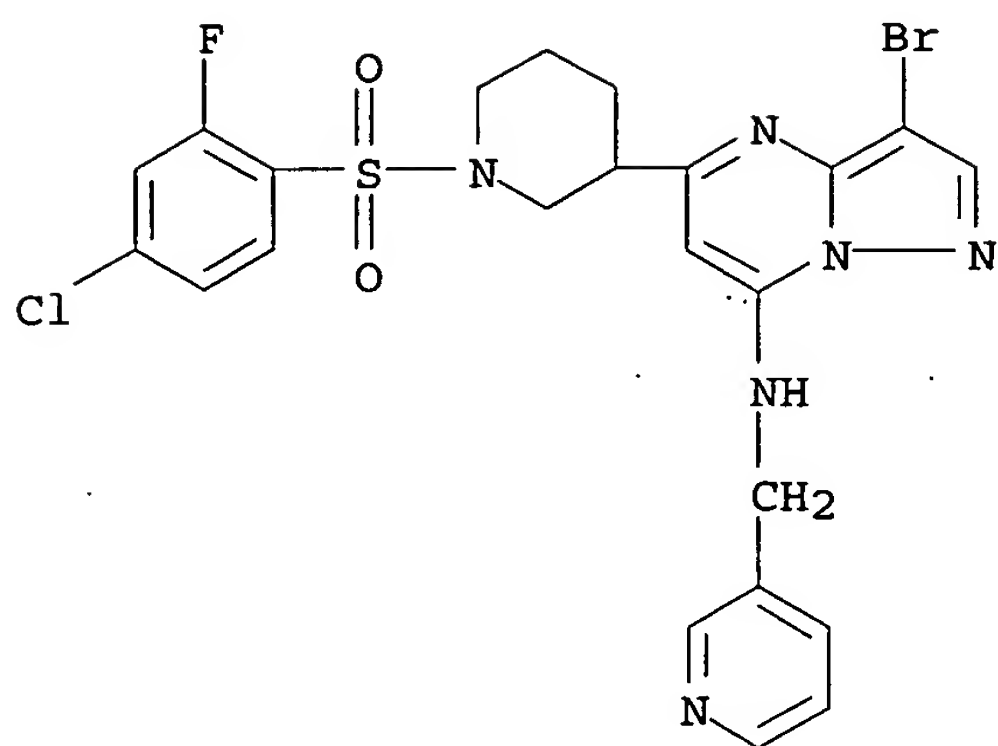
RN 677794-41-1 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylpropyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



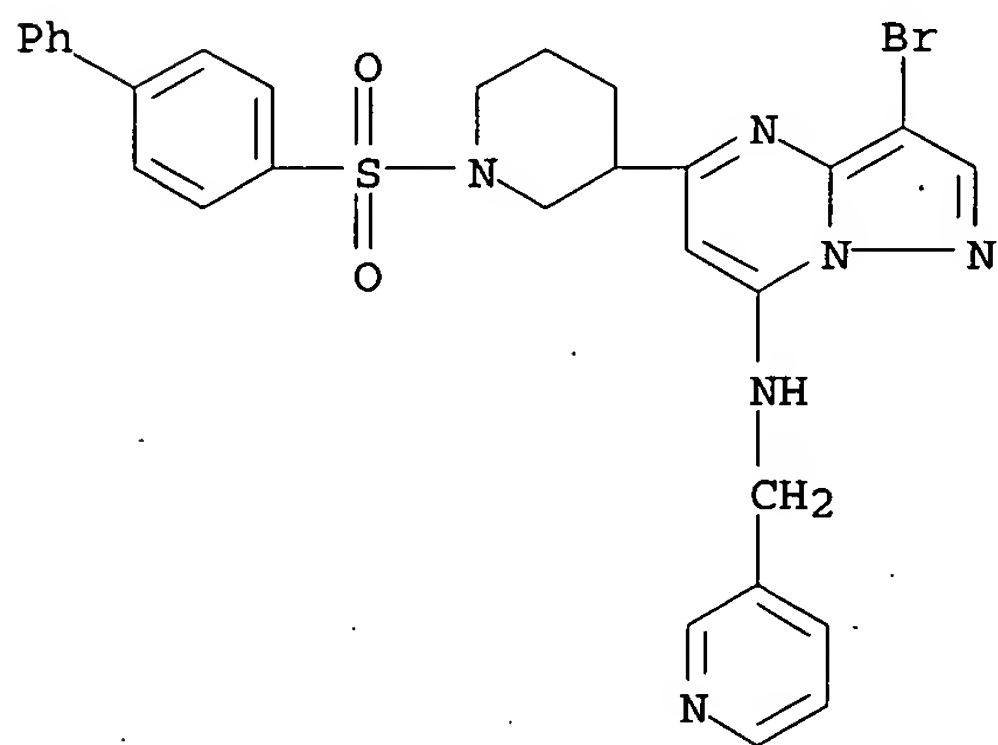
RN 677794-42-2 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chloro-2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



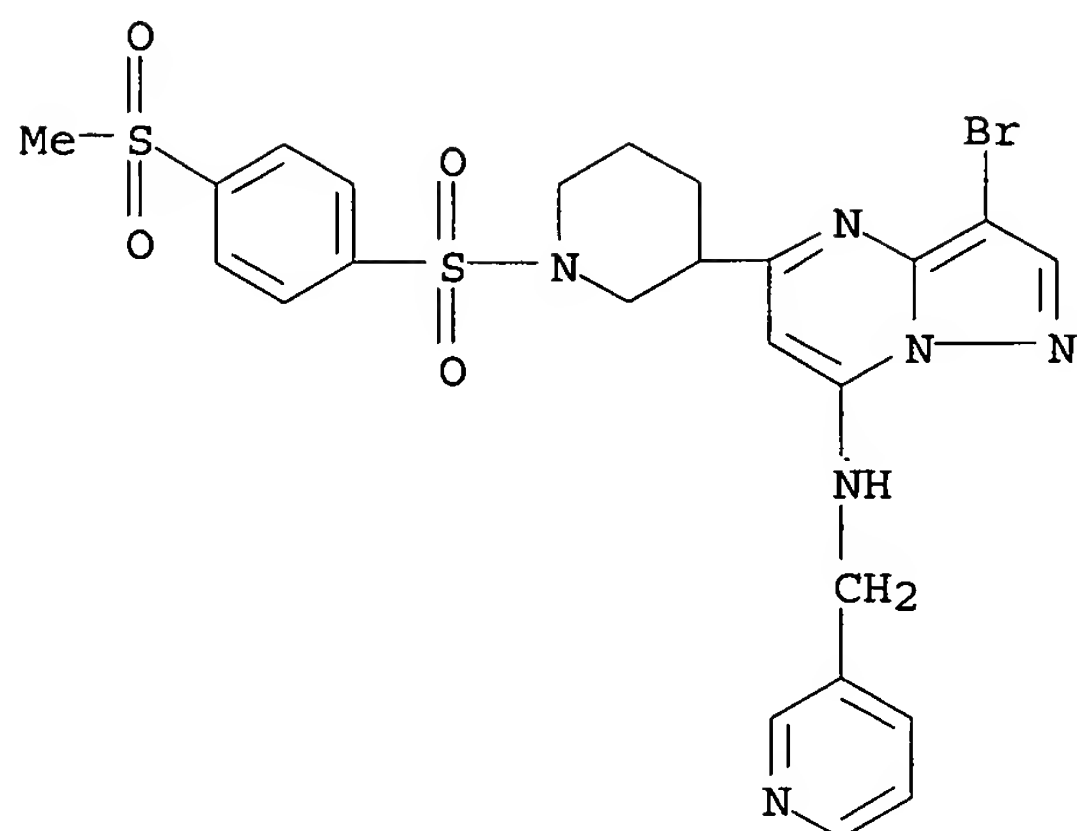
RN 677794-43-3 HCAPLUS

CN Piperidine, 1-([1,1'-biphenyl]-4-ylsulfonyl)-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



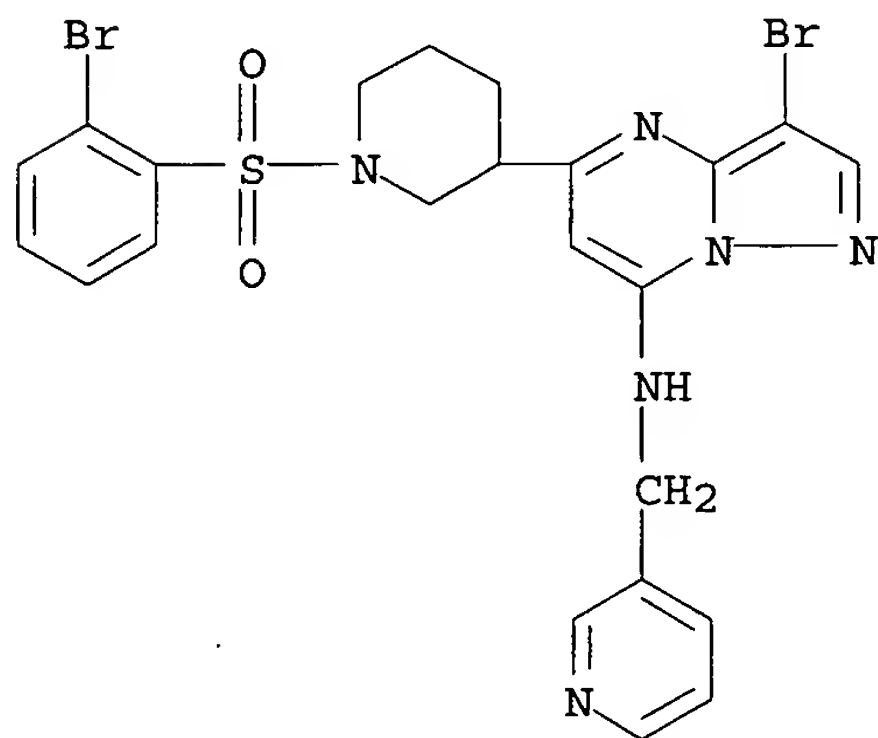
RN 677794-44-4 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



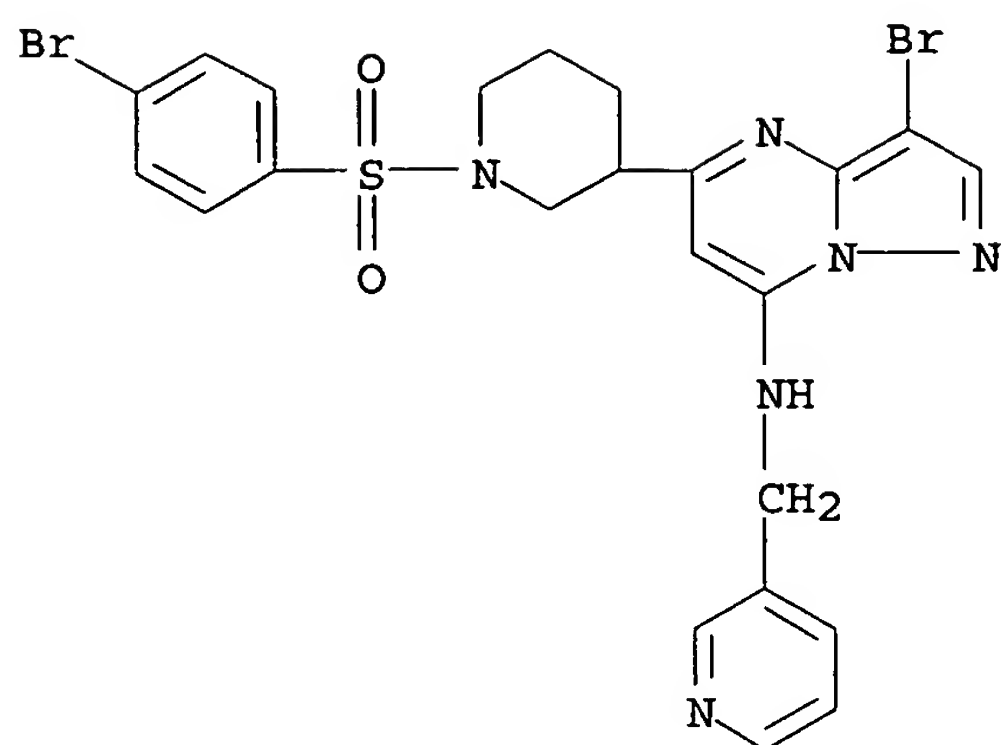
RN 677794-45-5 HCAPLUS

CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

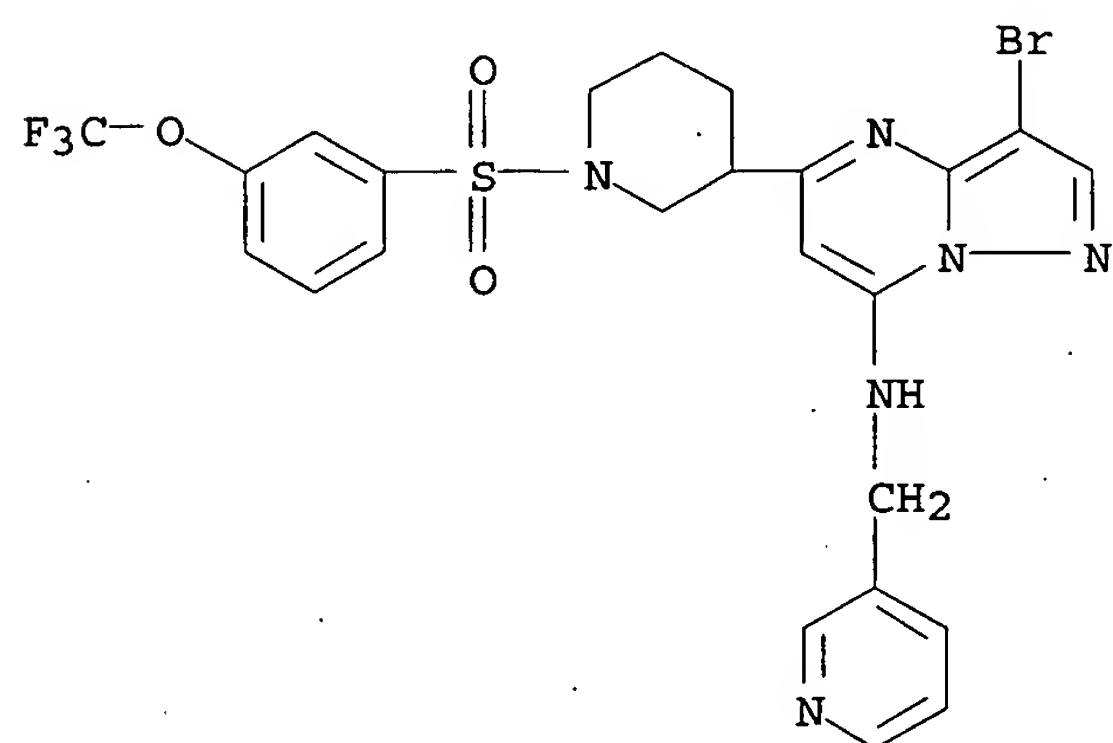


RN 677794-46-6 HCAPLUS

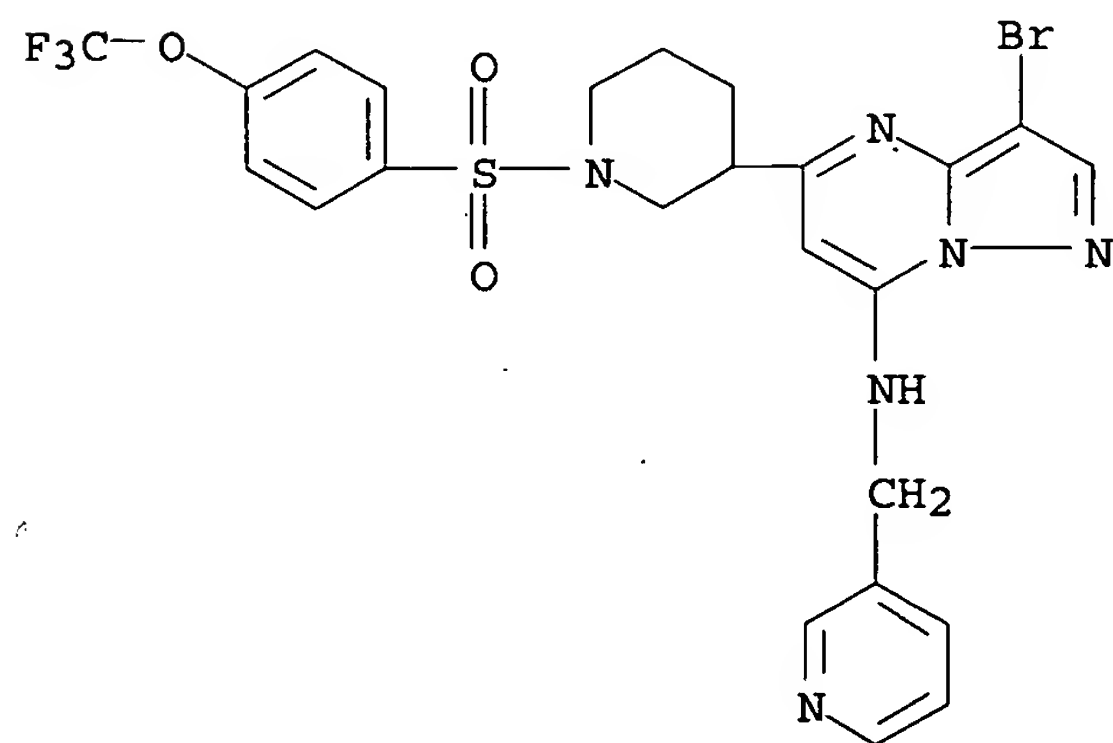
CN Piperidine, 1-[(4-bromophenyl)sulfonyl]-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



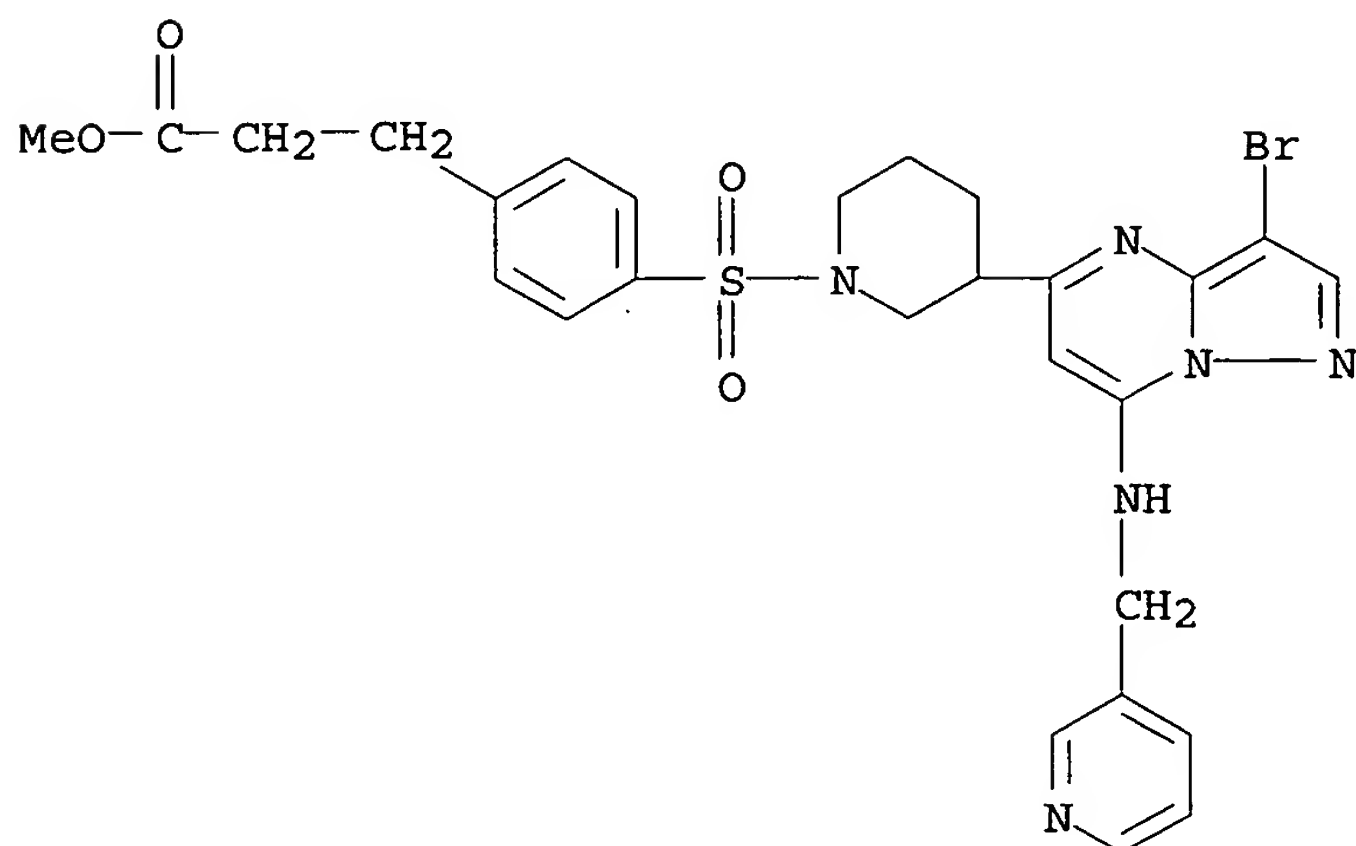
RN 677794-47-7 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



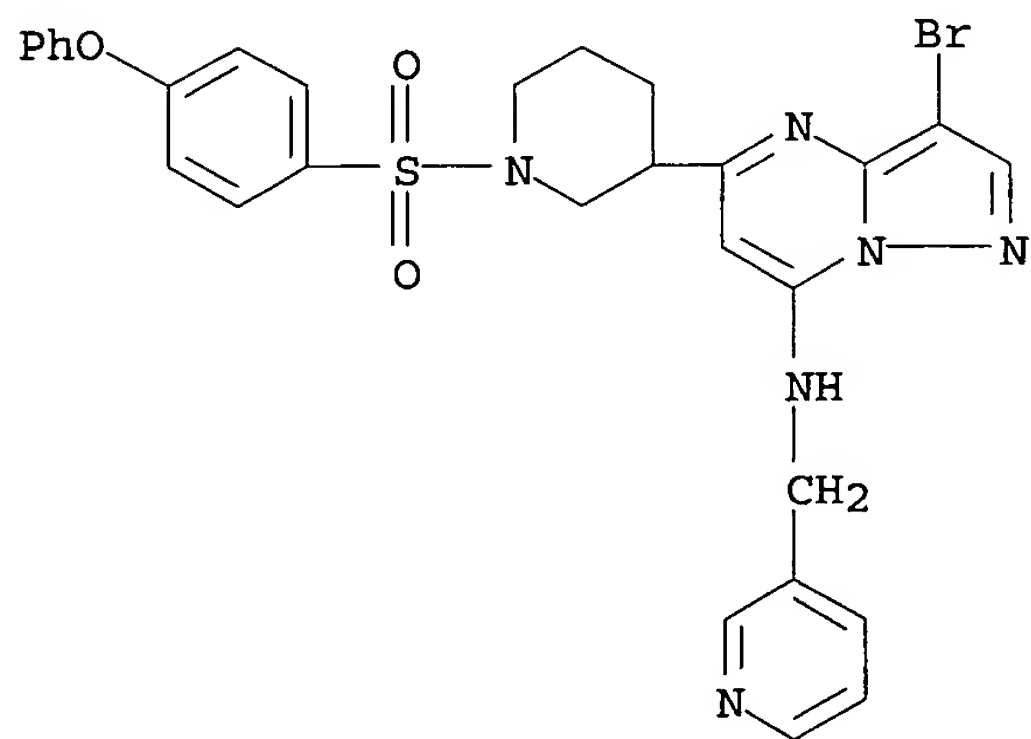
RN 677794-48-8 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-49-9 HCAPLUS  
 CN Benzenepropanoic acid, 4-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

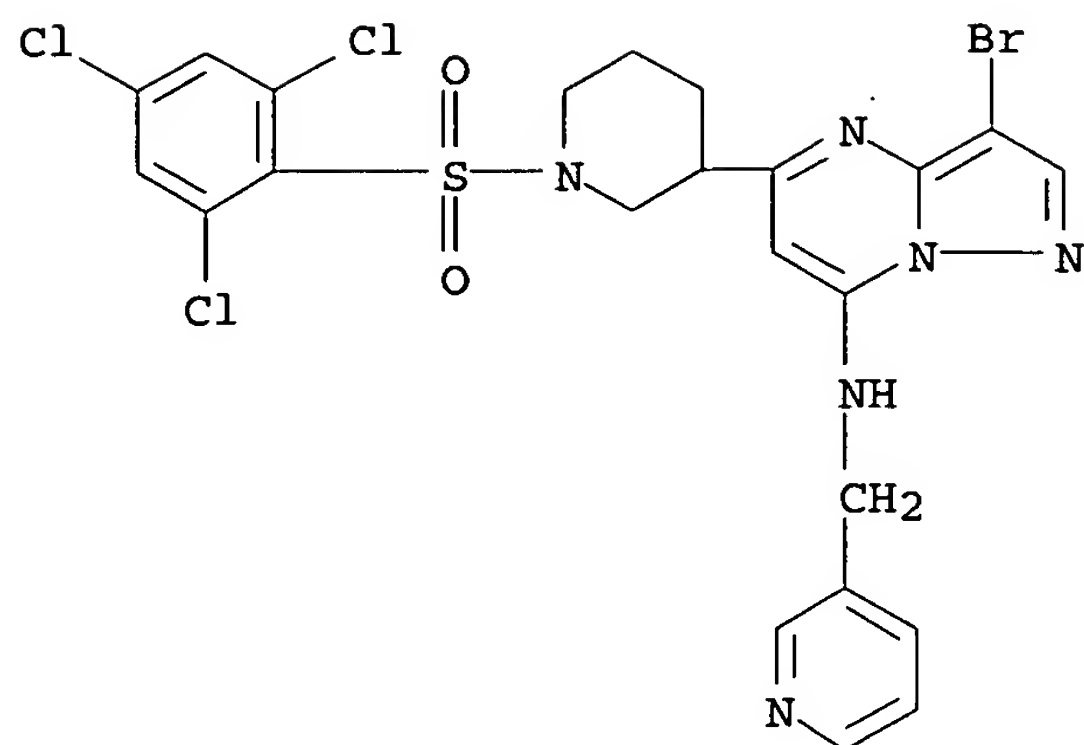


RN 677794-50-2 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-phenoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



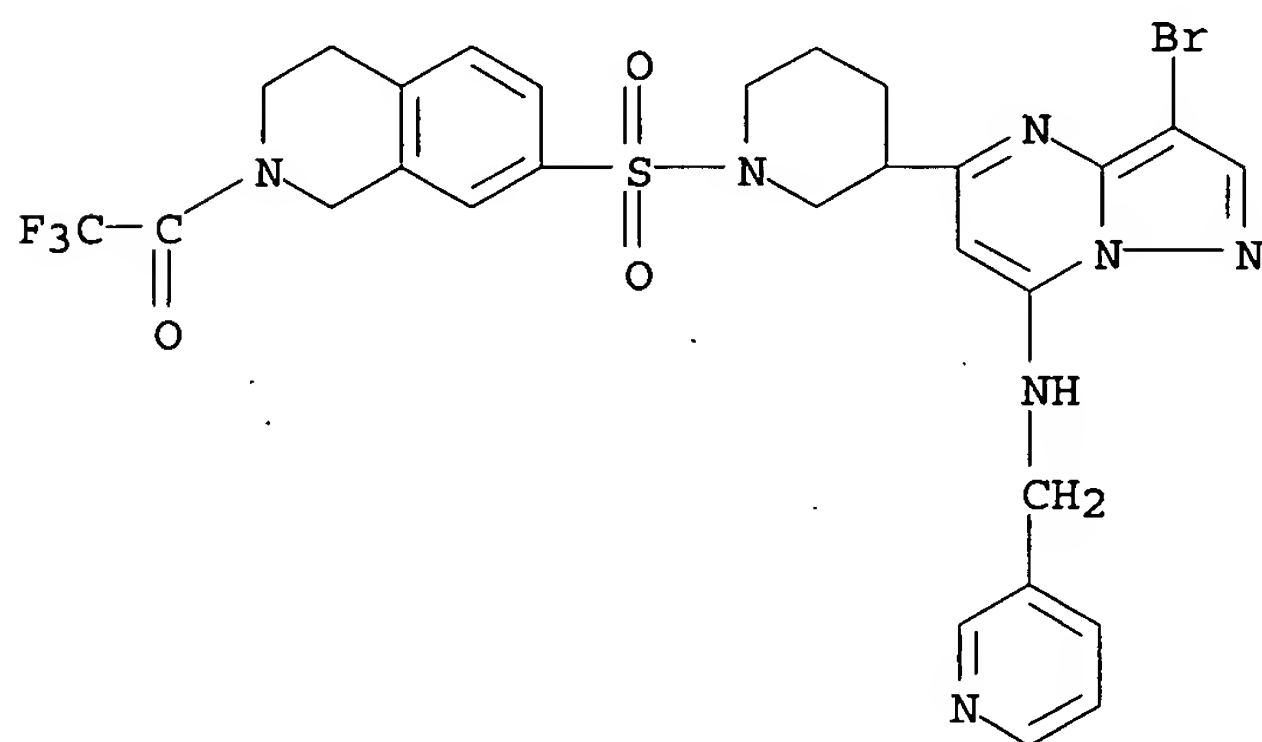
RN 677794-51-3 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)





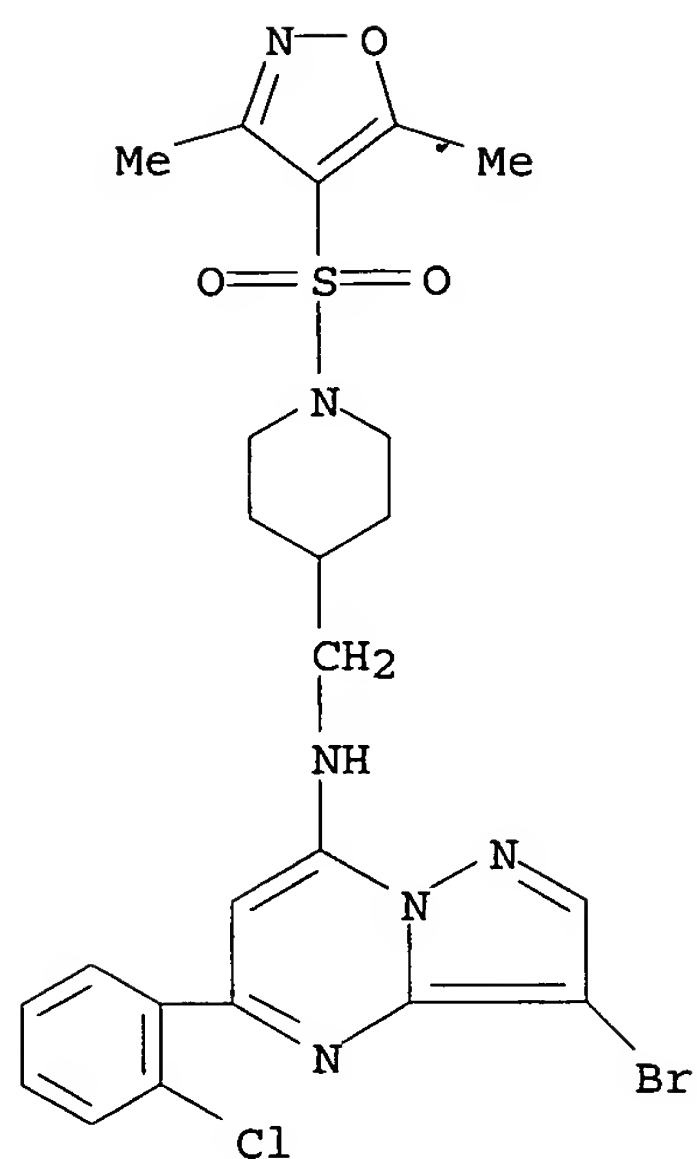
RN 677794-52-4 HCAPLUS

CN Isoquinoline, 7-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-1,2,3,4-tetrahydro-2-(trifluoroacetyl)-(9CI) (CA INDEX NAME)



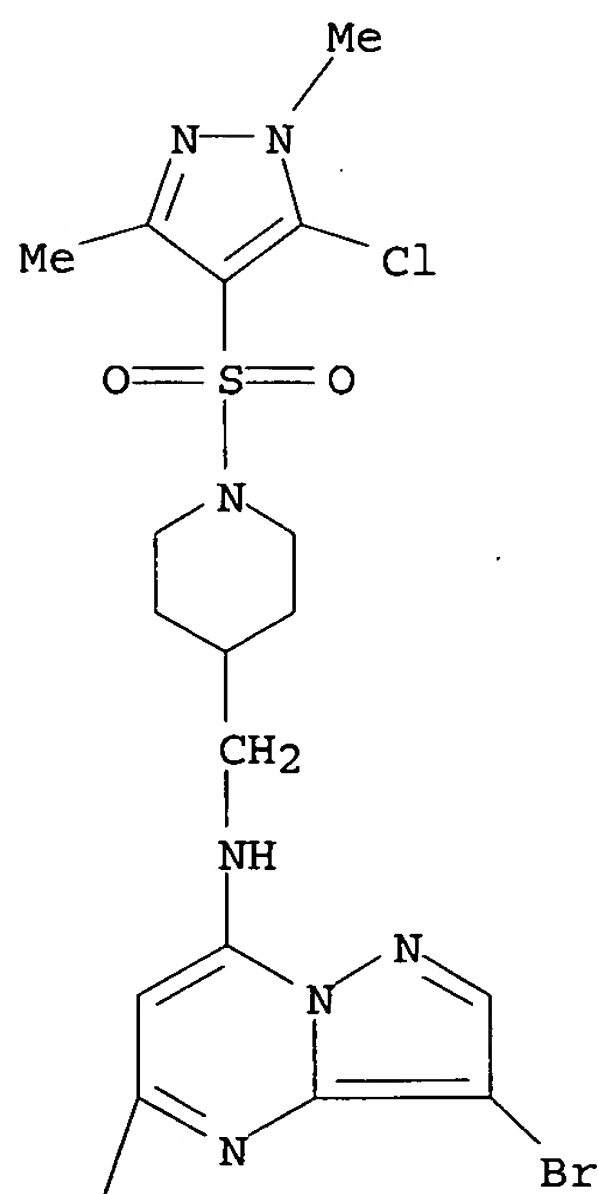
RN 677795-96-9 HCAPLUS

CN 4-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-(9CI) (CA INDEX NAME)

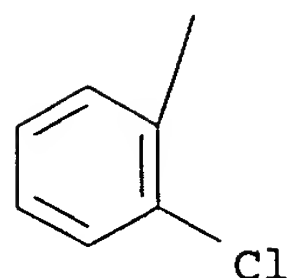


RN 677796-21-3 HCAPLUS  
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 (9CI) (CA INDEX NAME)

PAGE 1-A

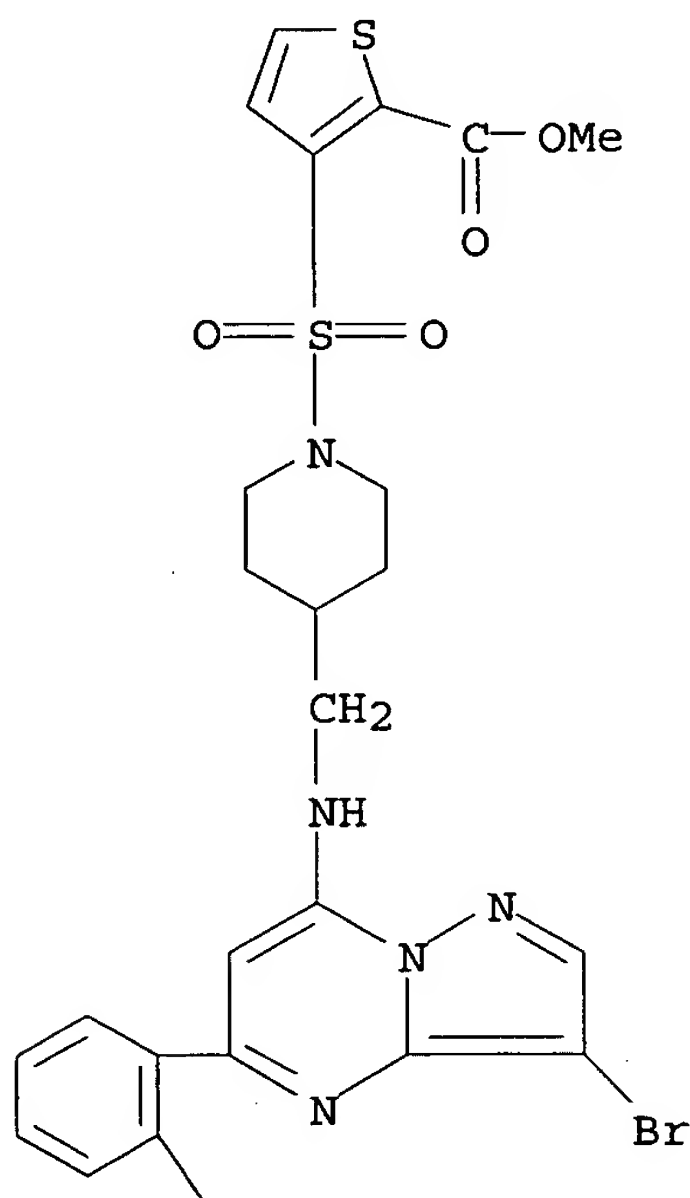


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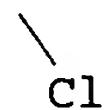


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PAGE 1-A



PAGE 2-A



L37 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:265849 HCAPLUS  
 DOCUMENT NUMBER: 140:321371  
 TITLE: Preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors  
 INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.; Doll, Ronald J.; Girjavallabhan, Viyyoor Moopil; Mallams, Alan; Alvarez, Carmen S.; Keertikar, Kartik

M.; Rivera, Jocelyn; Chan, Tin-yau; Madison, Vincent;  
 Fischmann, Thierry O.; Dillard, Lawrence W.; Tran,  
 Vinh D.; He, Zhen Min; James, Ray Anthony; Park,  
 Haengsoon; Paradkar, Vidyadhar M.; **Hobbs, Douglas  
 Walsh**

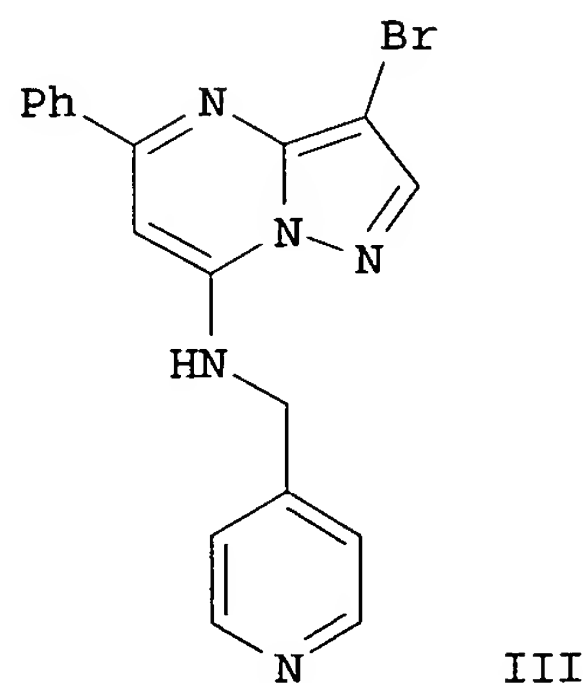
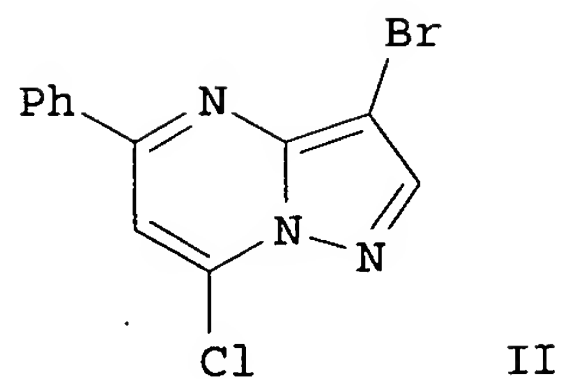
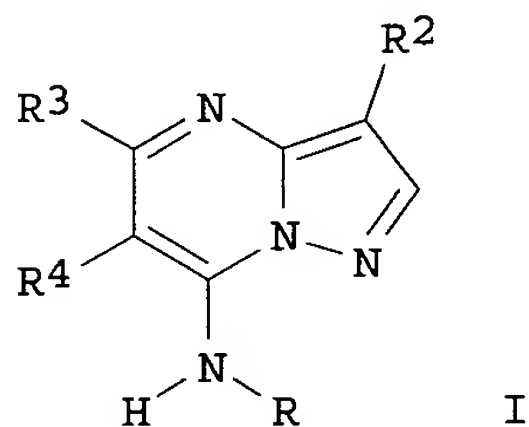
PATENT ASSIGNEE(S): Schering Corporation, USA  
 SOURCE: PCT Int. Appl., 609 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

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WO 2004022561	A1	20040318	WO 2003-XB27555	20030903
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PRIORITY APPLN. INFO.:

US 2002-408027P P 20020904  
 US 2002-421959P P 20021029

GI



AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with 4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020  $\mu$ M and 0.029  $\mu$ M against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a

Part

III of I-III series.

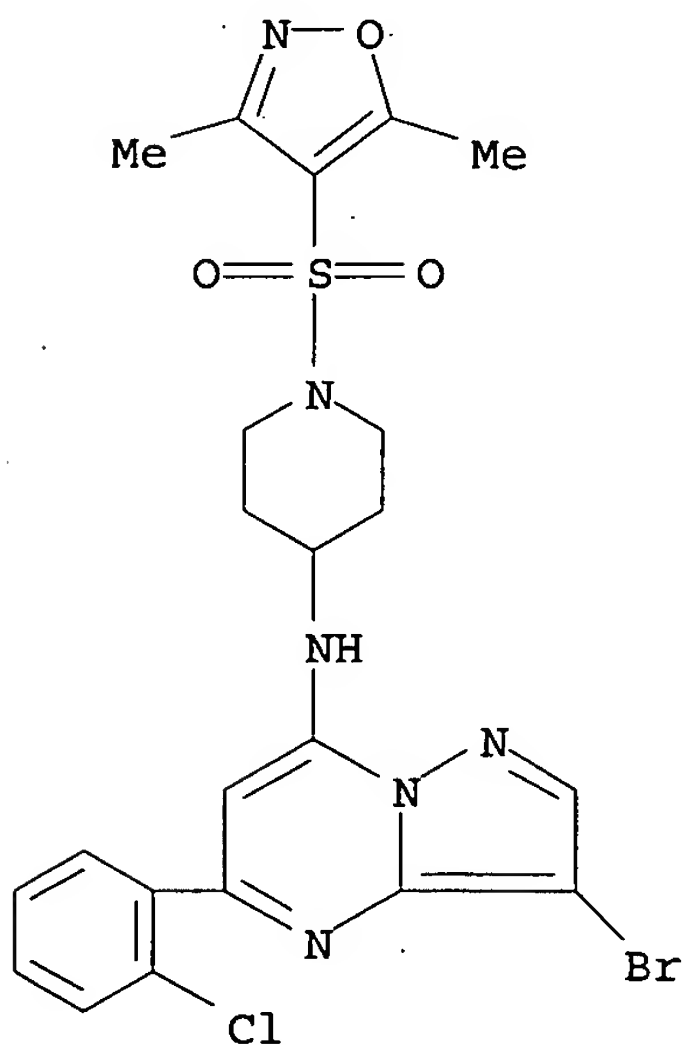
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RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors for treating cancer)

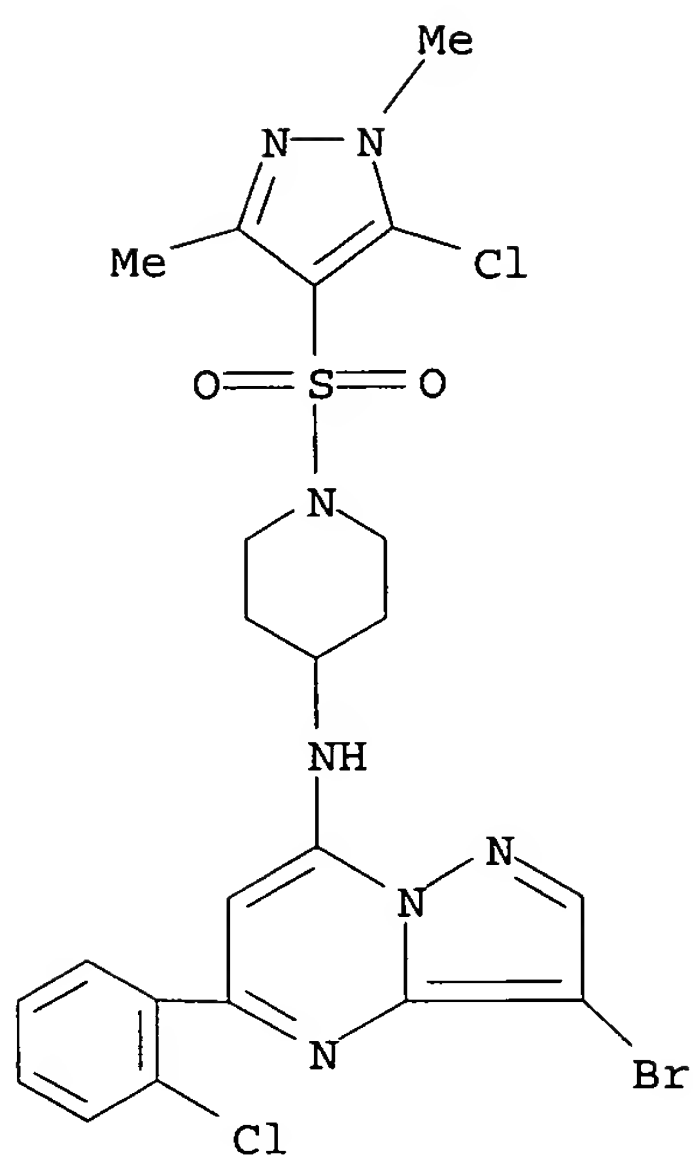
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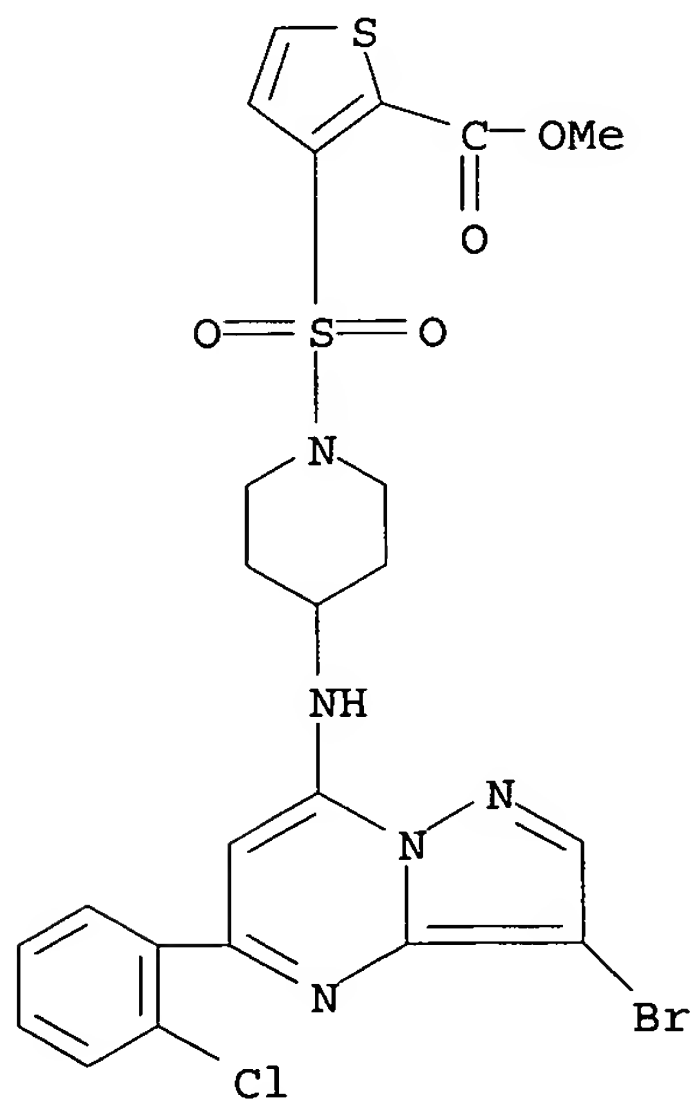
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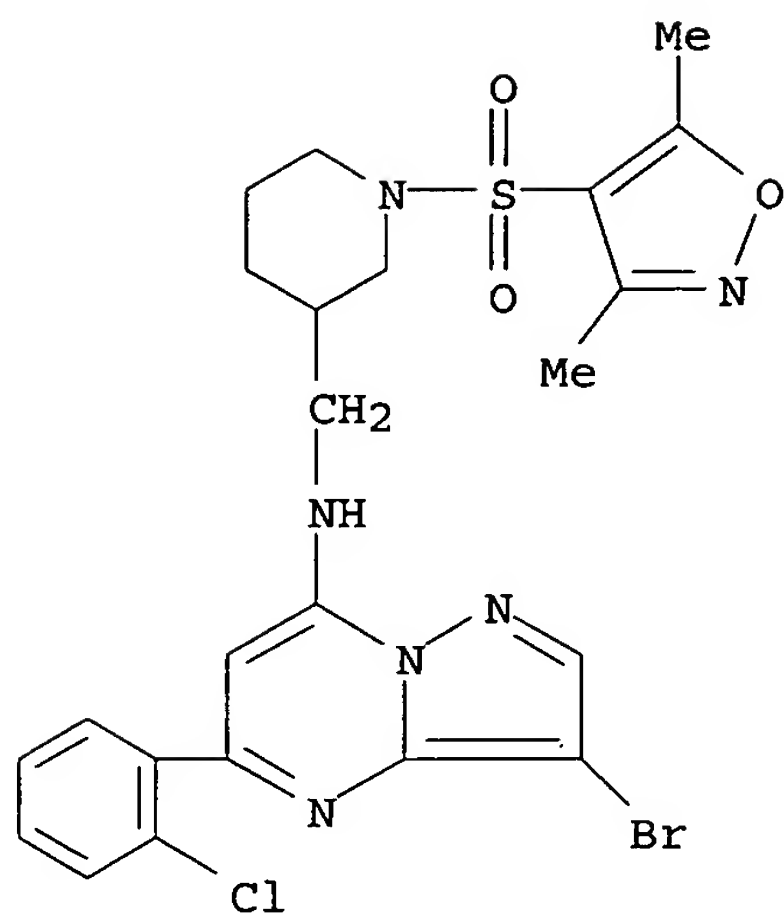
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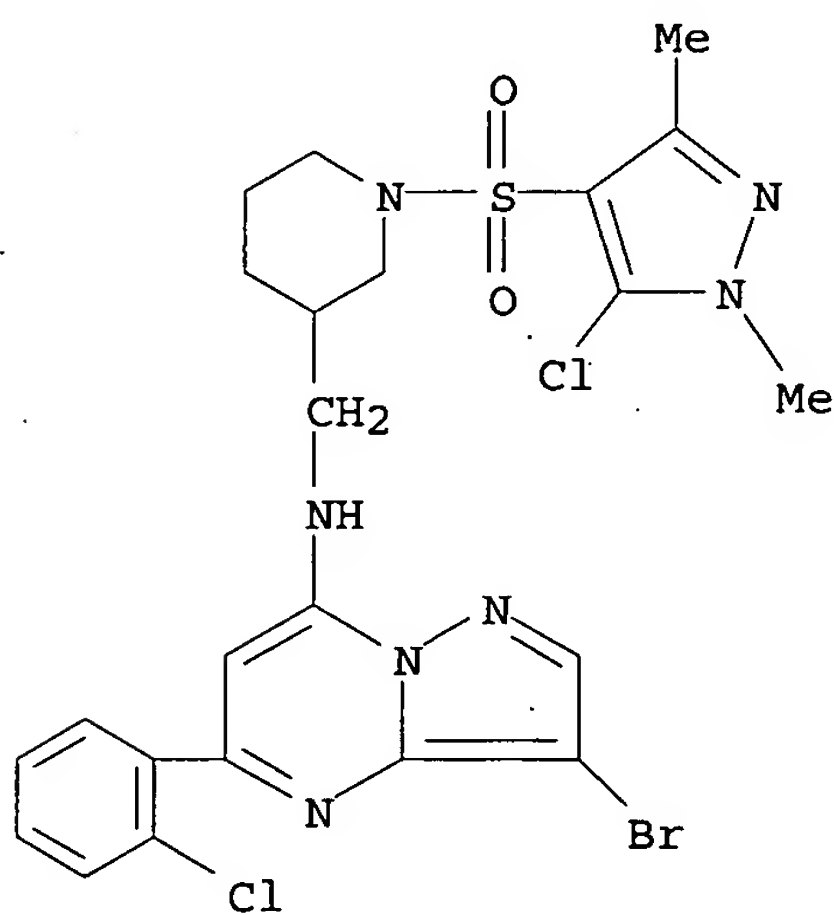
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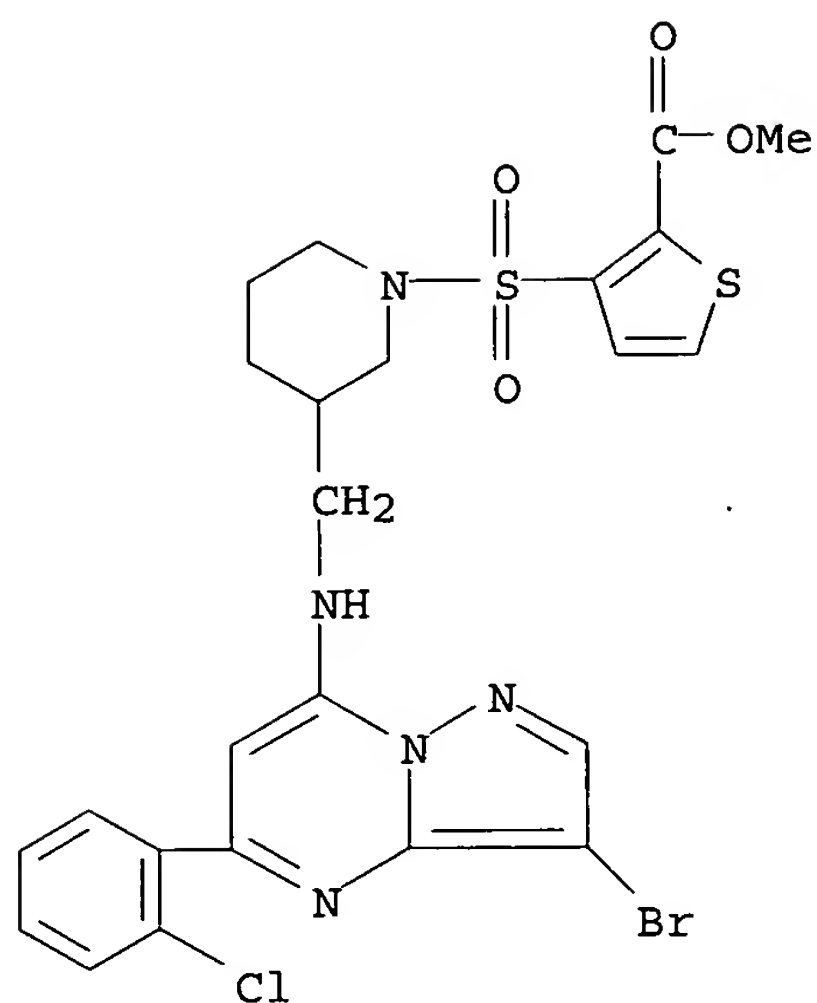
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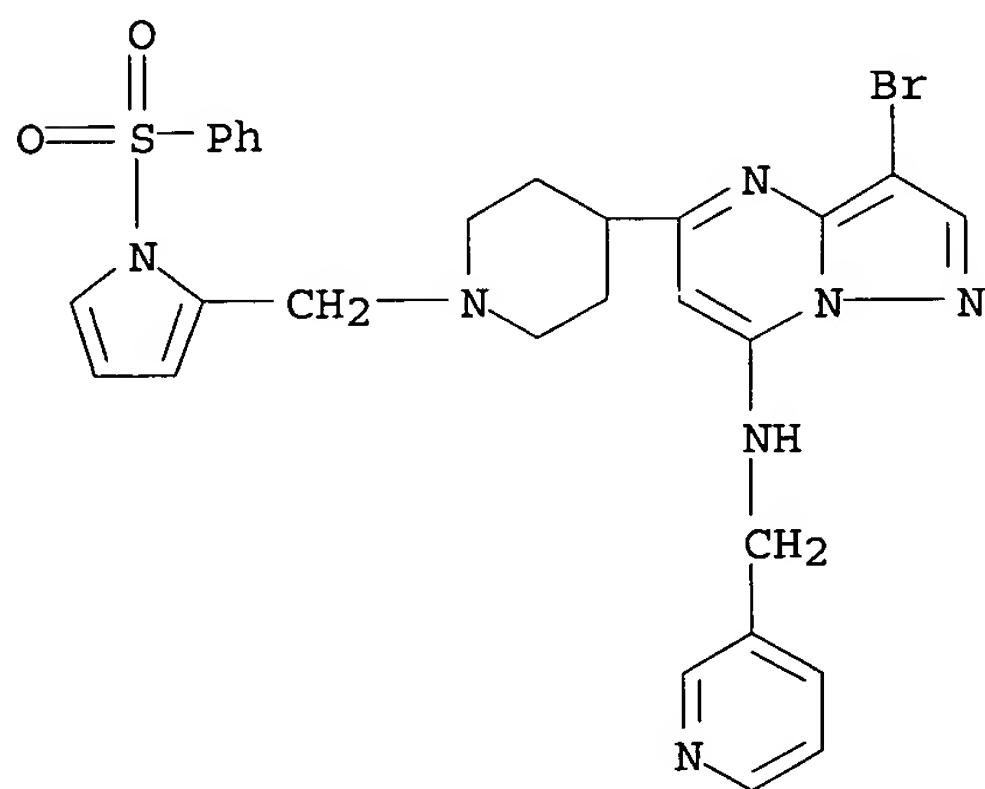


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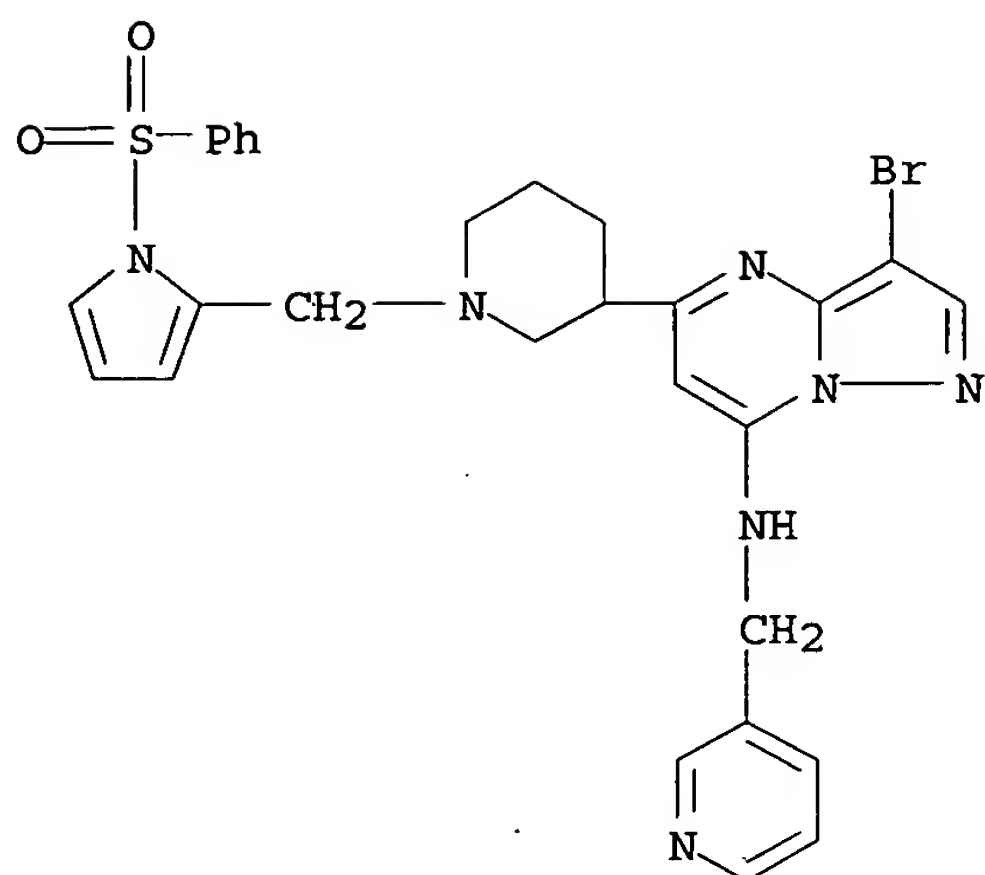


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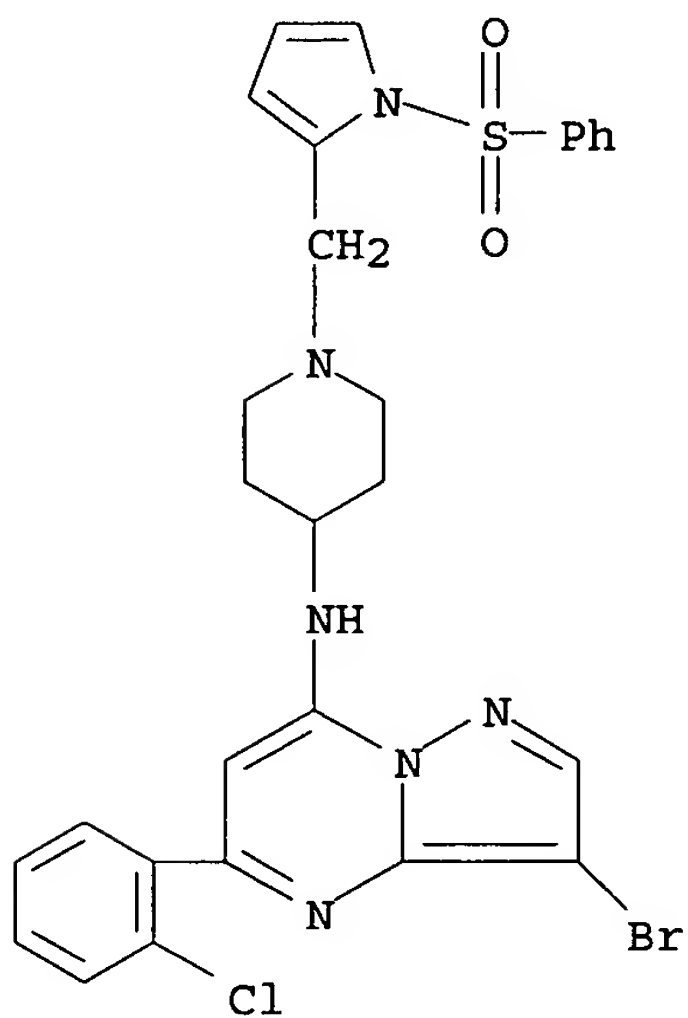
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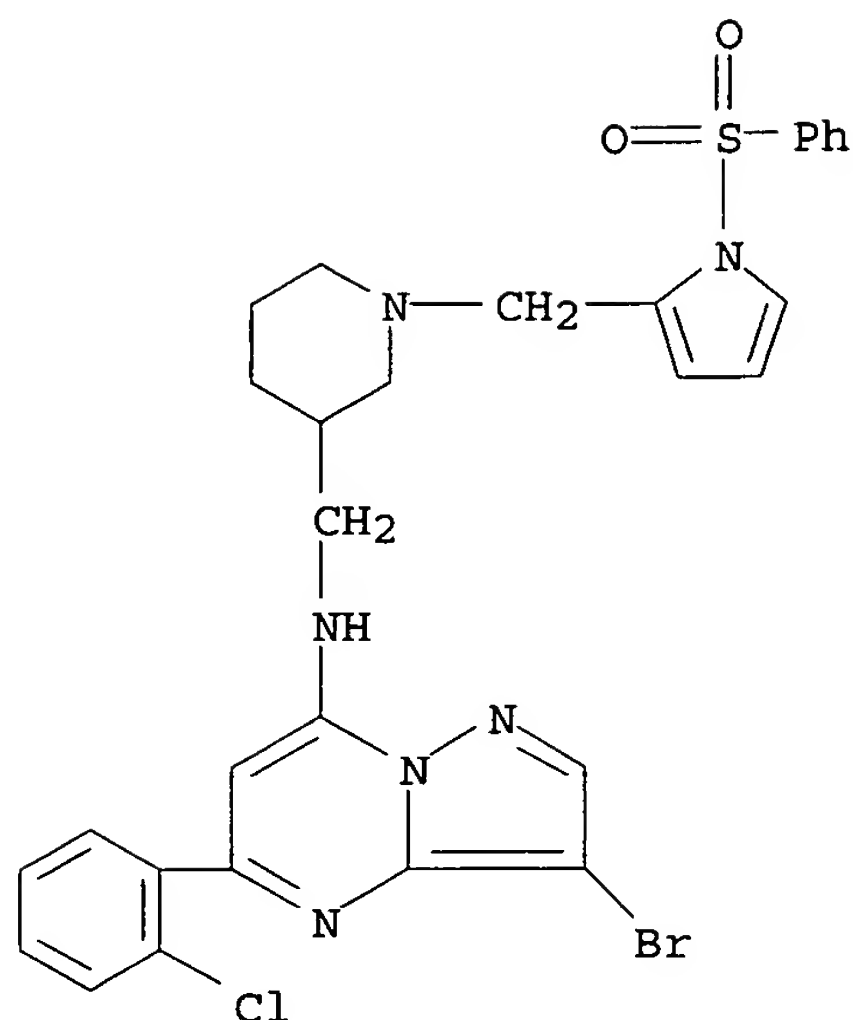
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L37 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:265847 HCAPLUS

DOCUMENT NUMBER: 140:321370

TITLE: Preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.; Doll, Ronald J.; Girijavallabhan, Viyyoor Moopil; Mallams, Alan; Alvarez, Carmen S.; Keertikar, Kartik M.; Rivera, Jocelyn; Chan, Tin-yau; Madison, Vincent; Fischmann, Thierry O.; Dillard, Lawrence W.; Tran, Vinh D.; He, Zhen Min; James, Ray Anthony; Park, Haengsoon; Paradkar, Vidyadhar M.; **Hobbs, Douglas Walsh**

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 609 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

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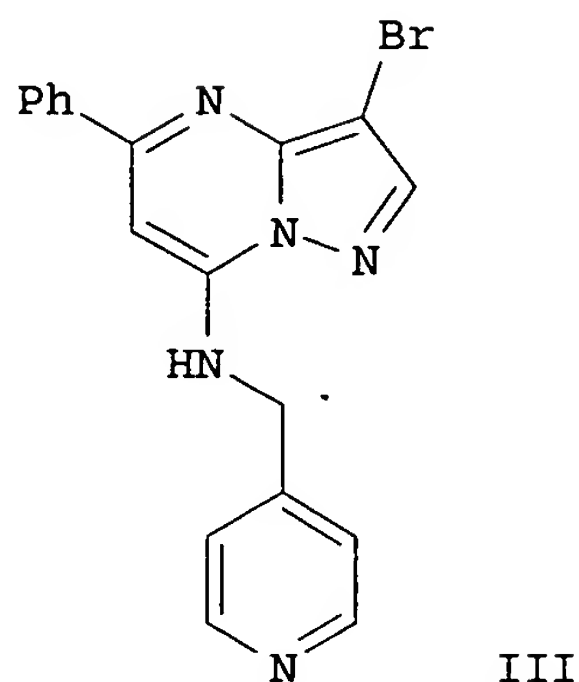
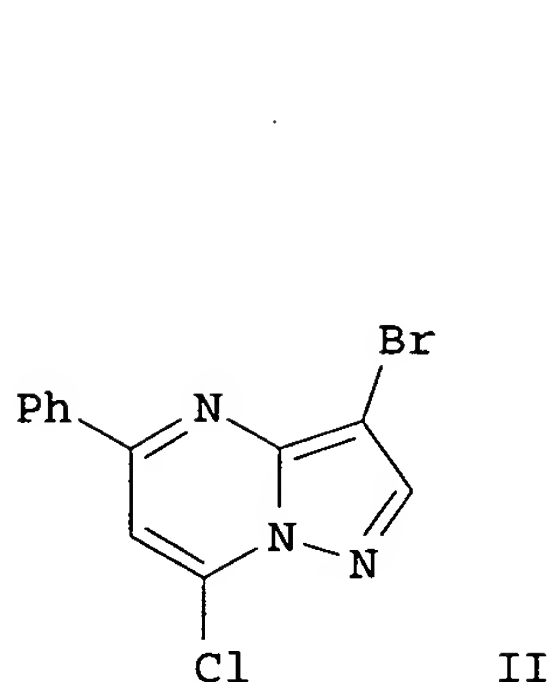
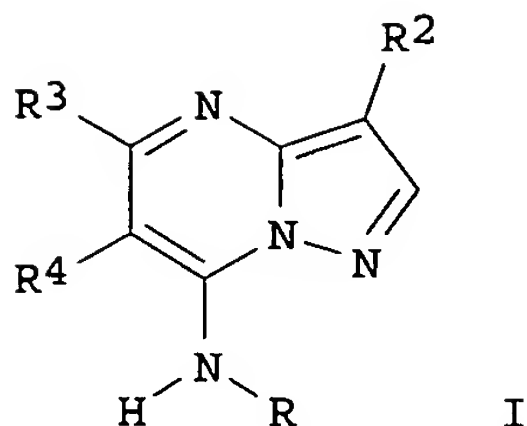
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PRIORITY APPLN. INFO.:

US 2002-408027P P 20020904

US 2002-421959P P 20021029

GI



AB The title compds. [I R = H, alkyl, cycloalkyl, etc.; R2 = alkyl, halo, aryl, etc.; R3 = H, halo, aryl, etc.; R4 = H, halo, alkyl], useful as inhibitors of cyclin dependent kinases for treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs such as cancer, were prepared Thus, reacting II (preparation given) with 4-aminomethylpyridine afforded 93% III which showed IC50 of 0.020  $\mu$ M and 0.029  $\mu$ M against CDK2 kinase (cyclin A or cyclin E-dependent). The pharmaceutical composition comprising the compound I is claimed. This is a

Part

II of I-III series.

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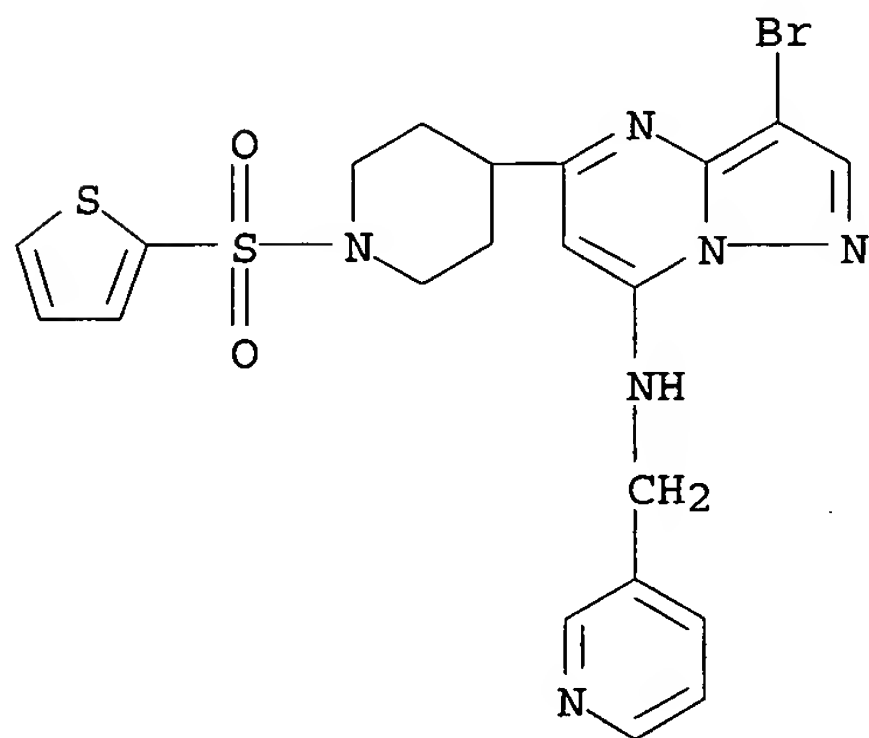
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RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU  
 (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study);  
 PREP (Preparation); USES (Uses)

(preparation of pyrazolopyrimidines as cyclin-dependent kinase inhibitors)

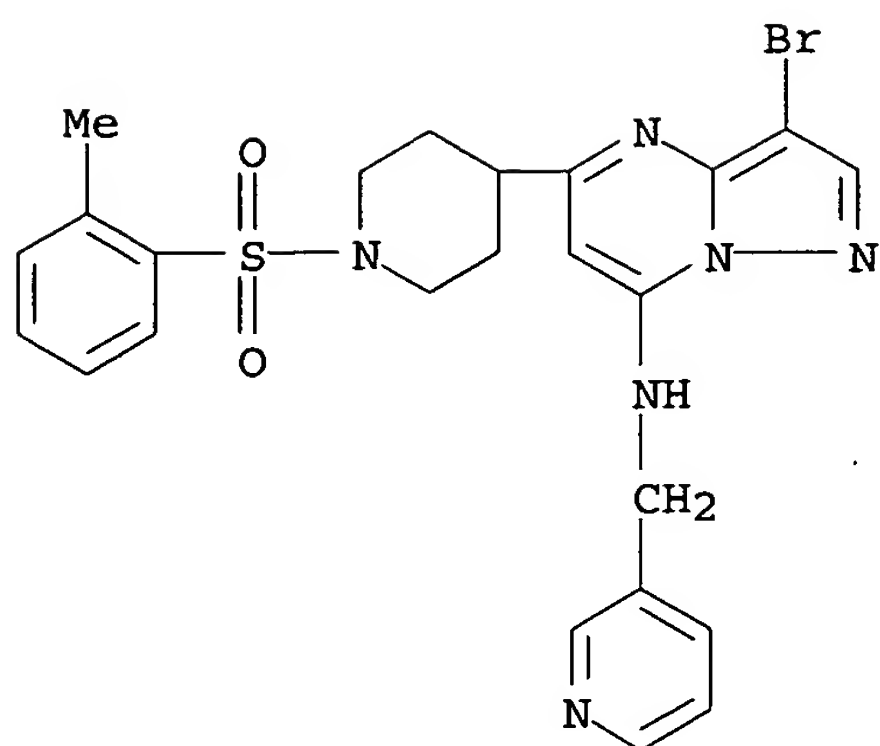
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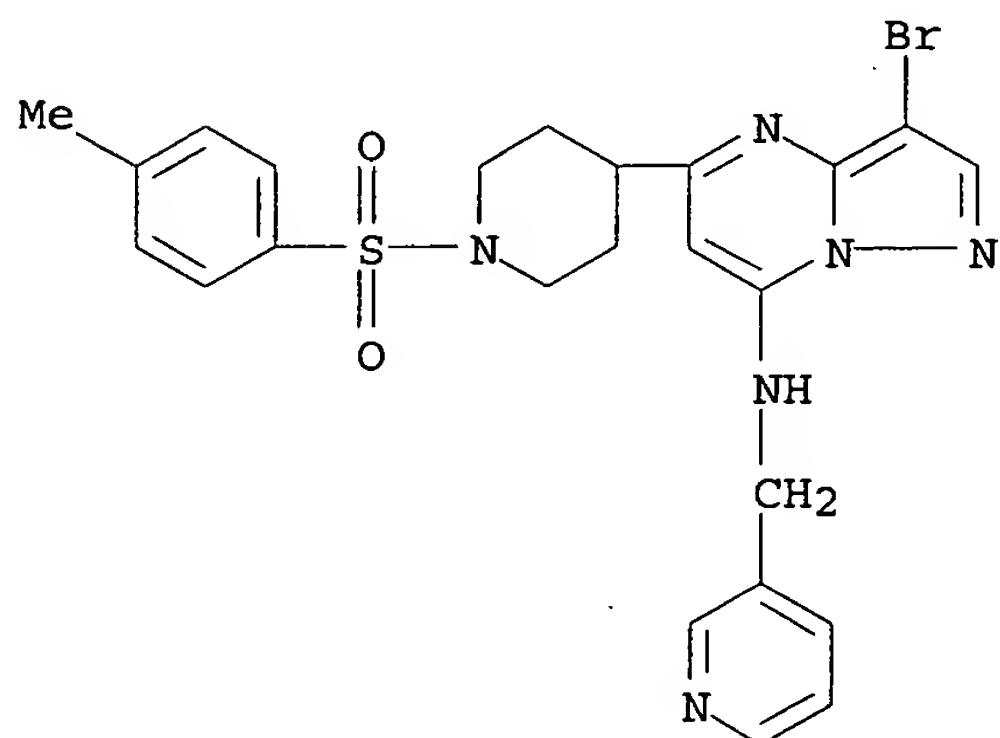
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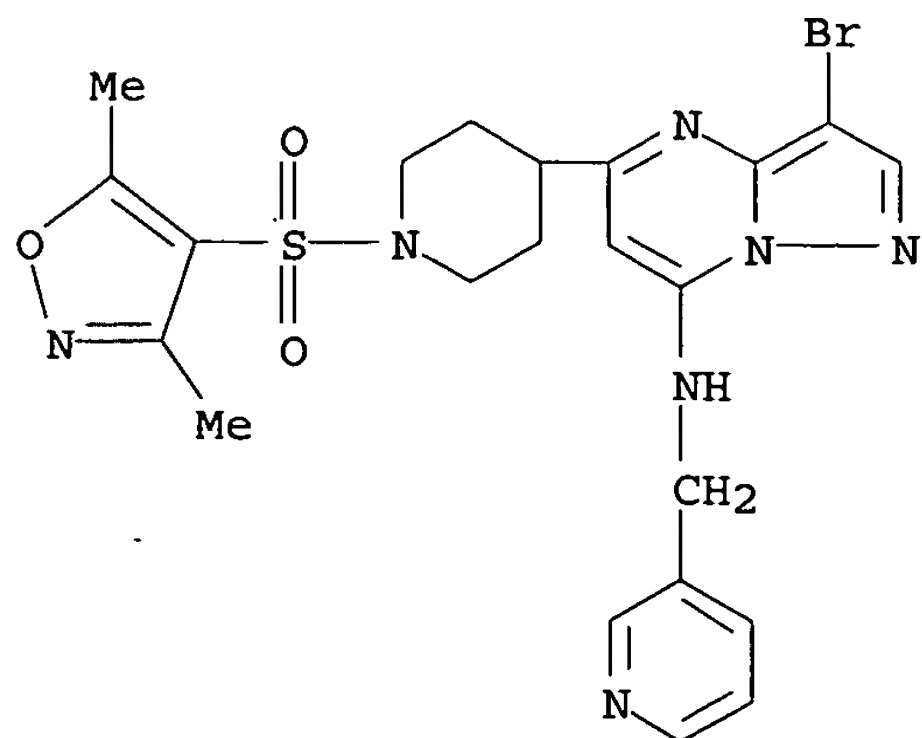
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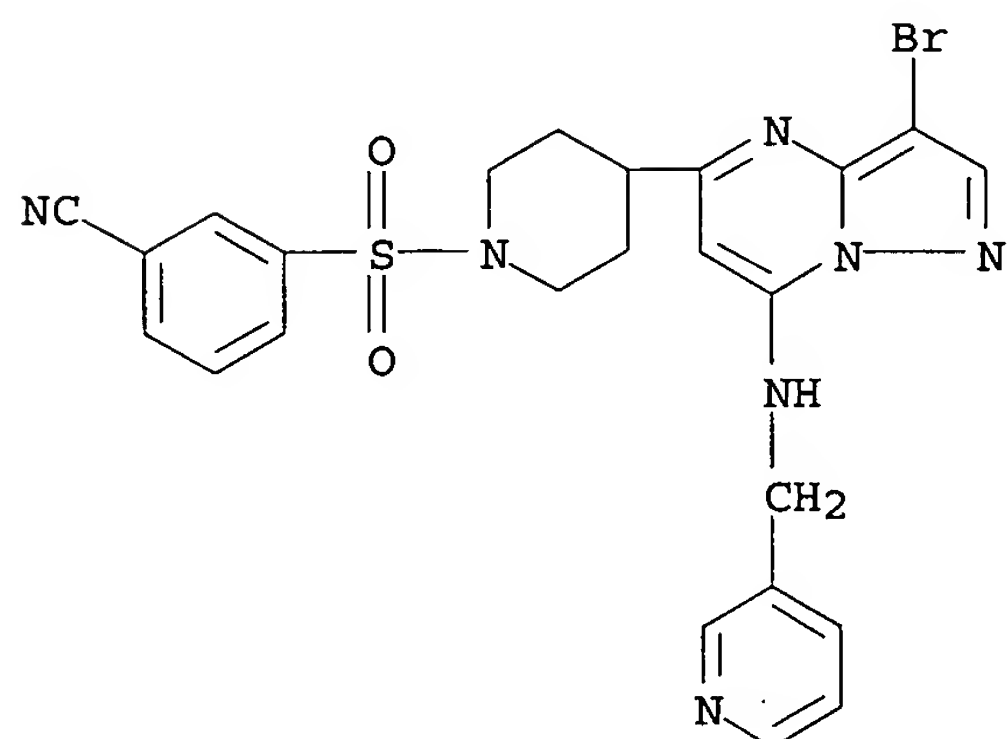
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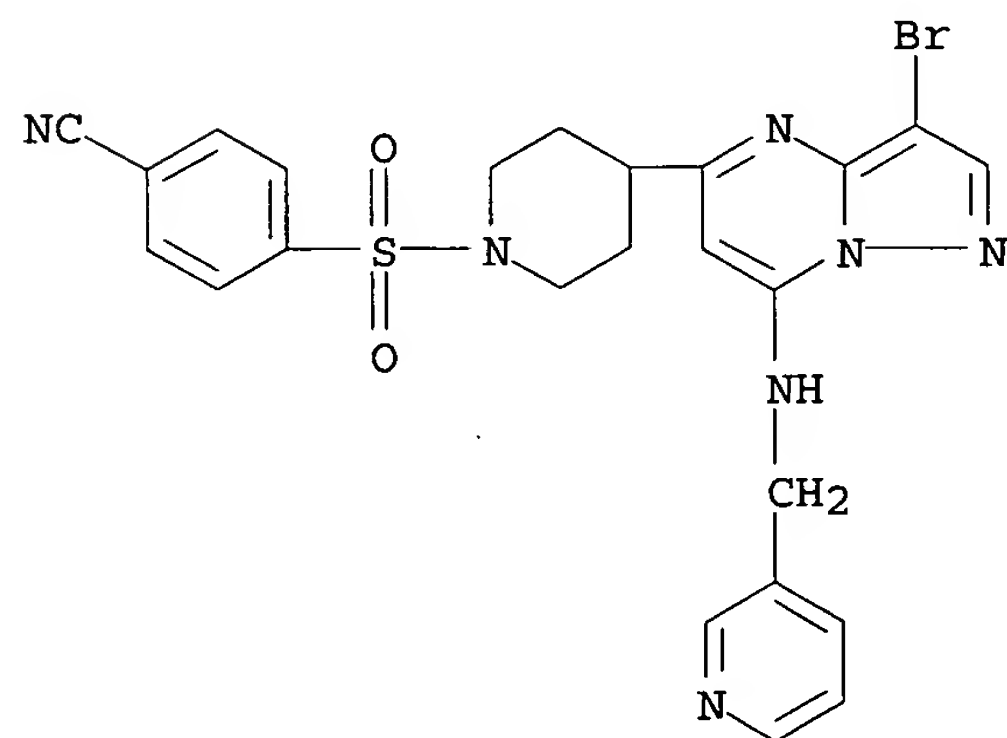
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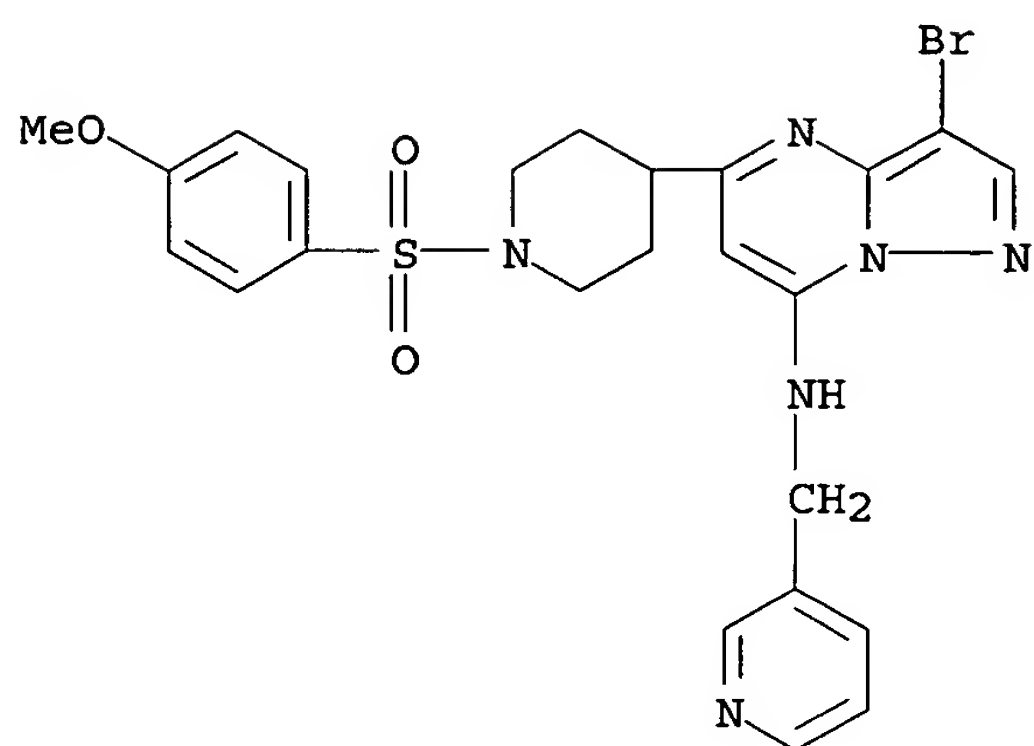
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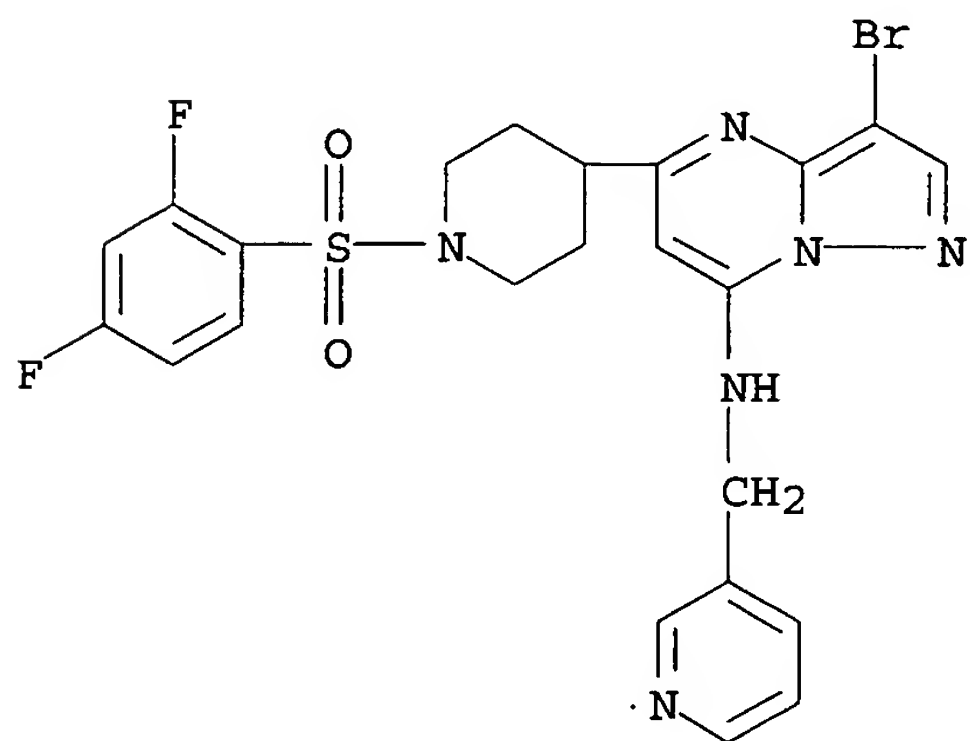
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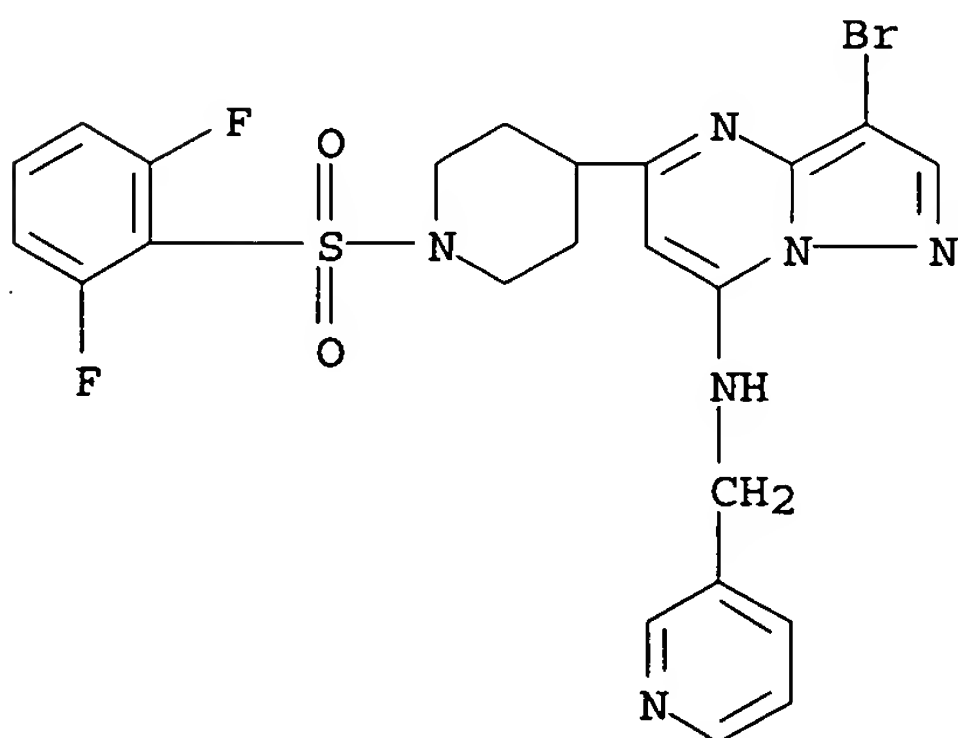
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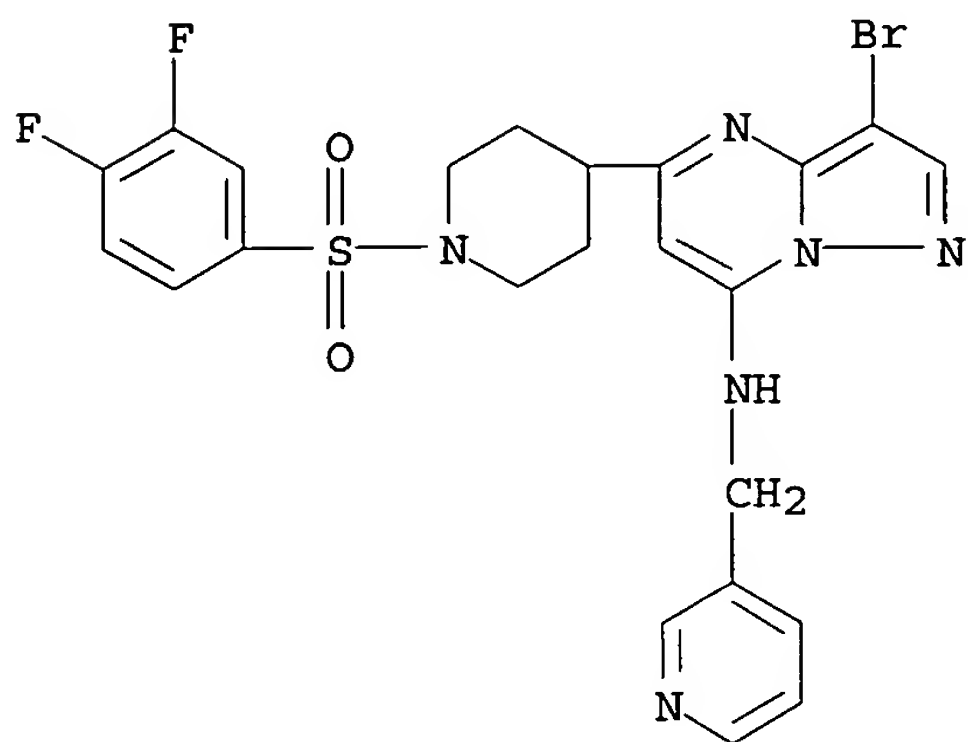
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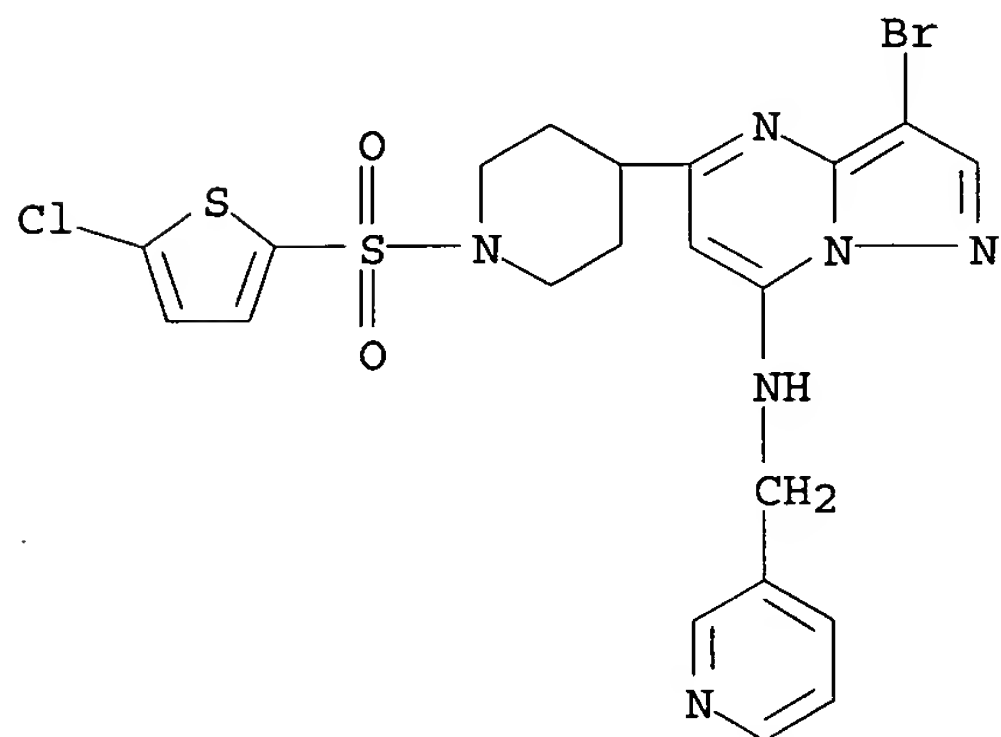


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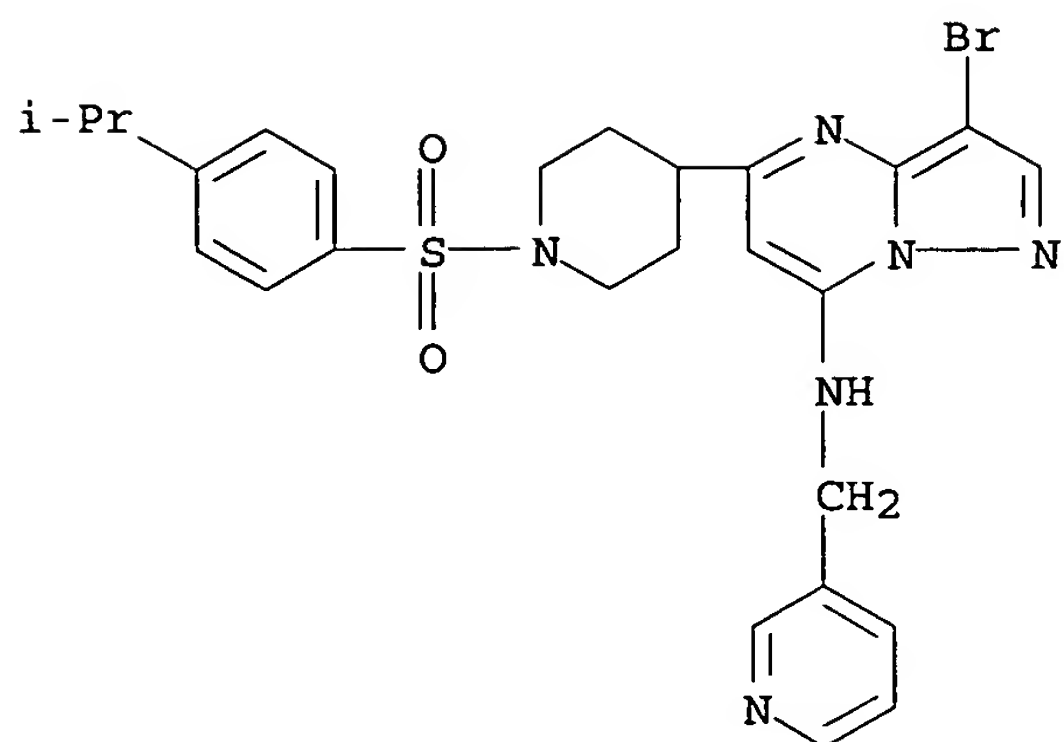


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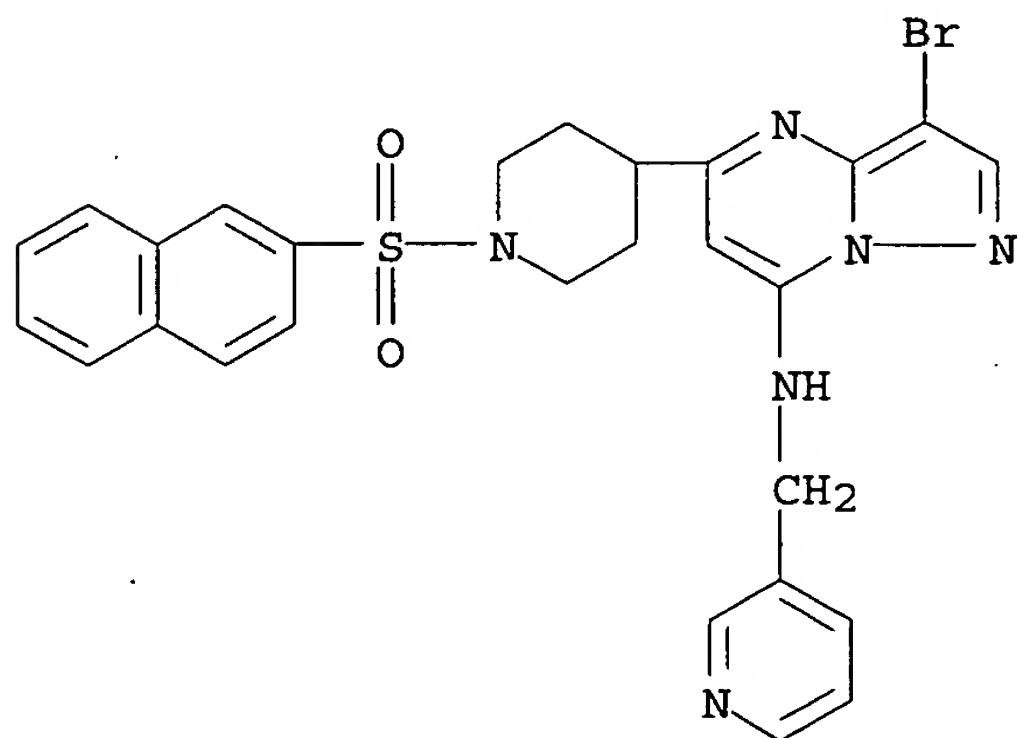
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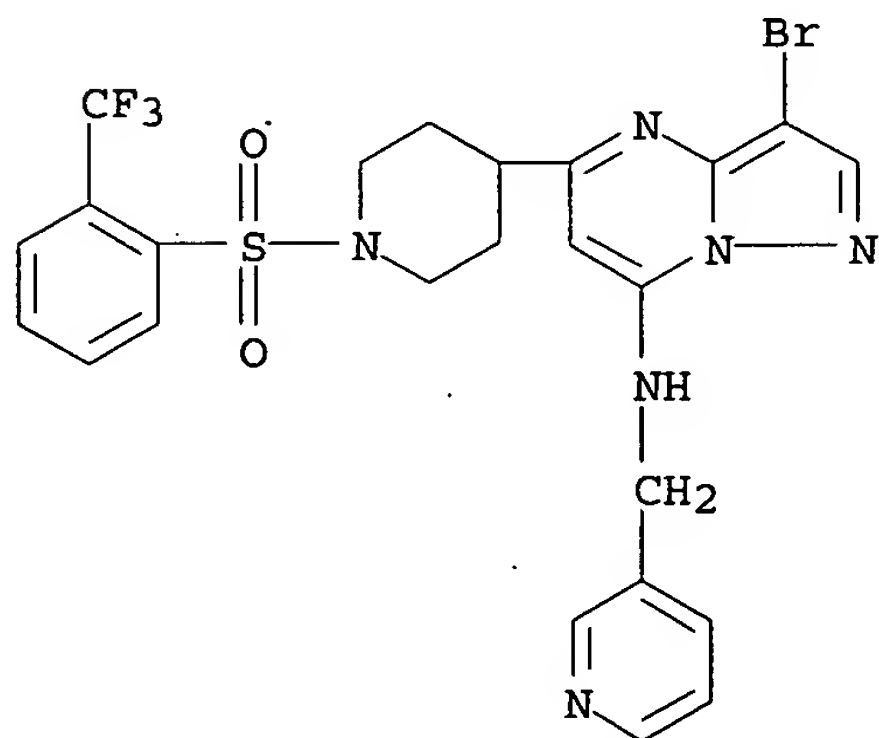
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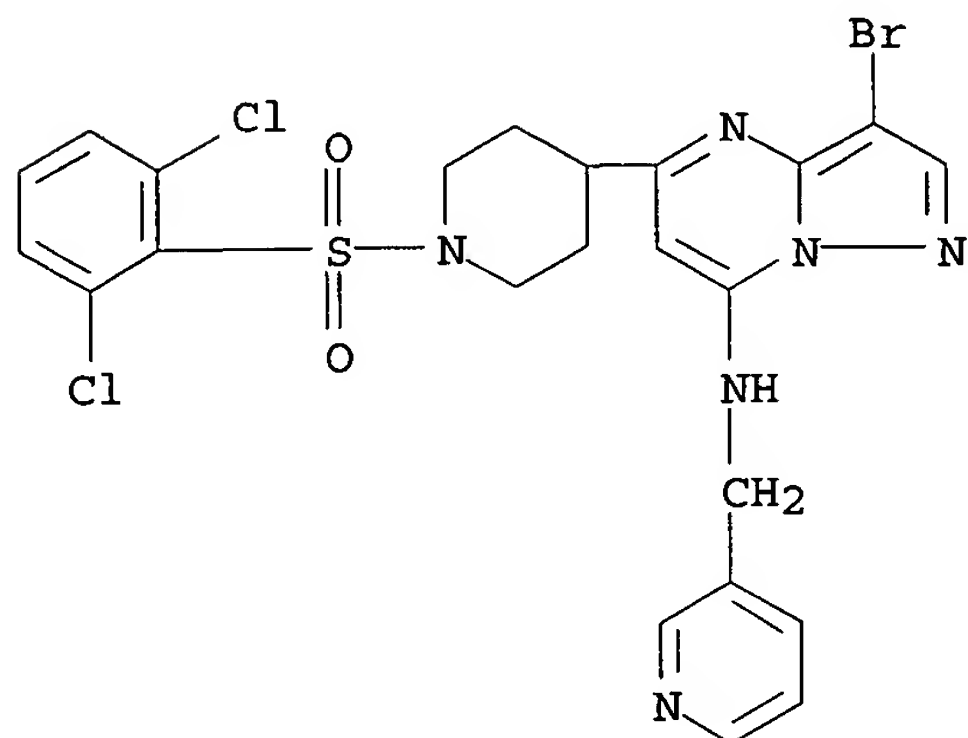


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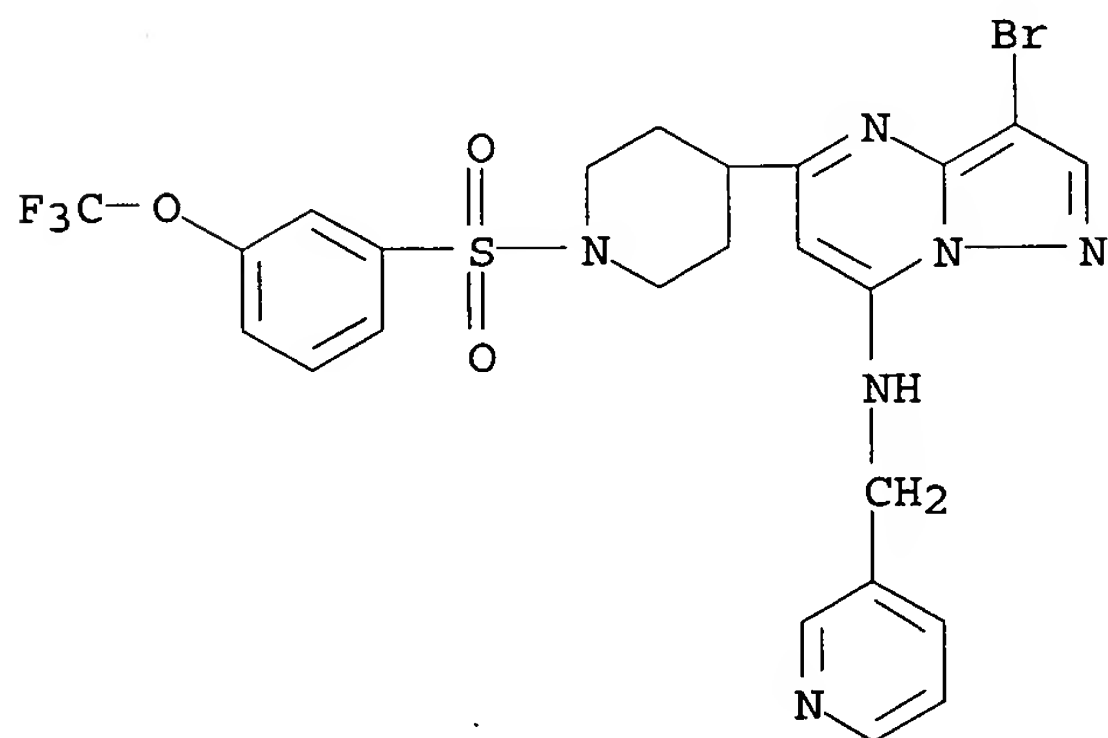
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



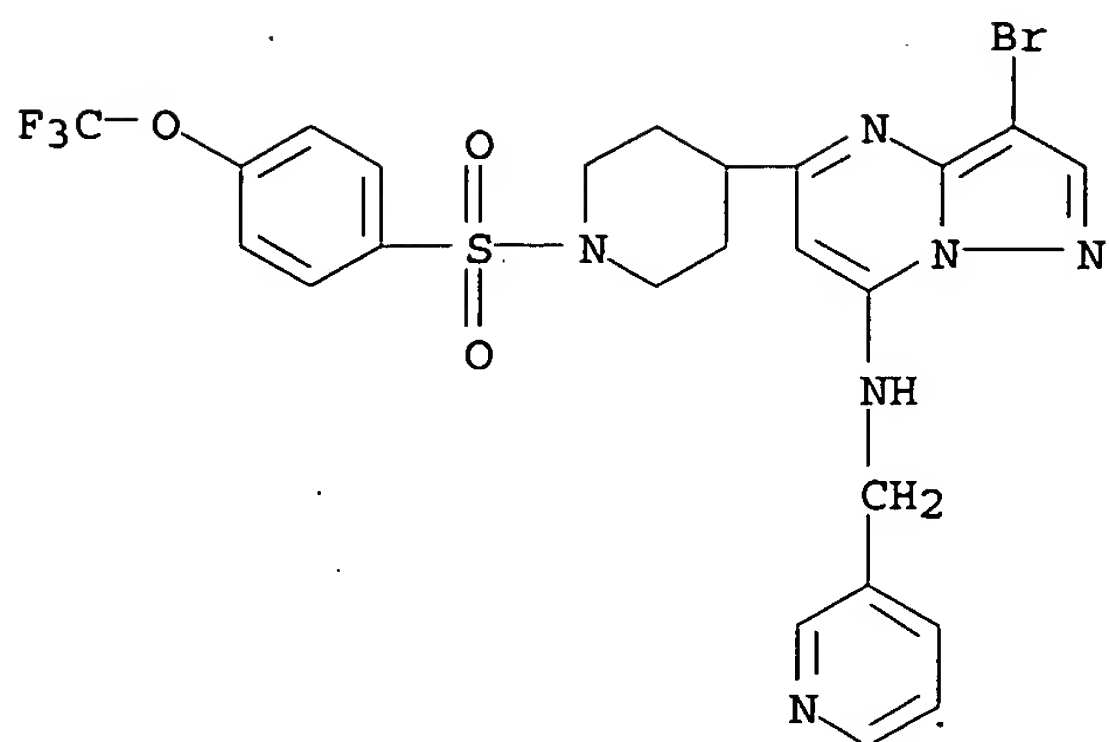
RN 677793-55-4 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677793-56-5 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

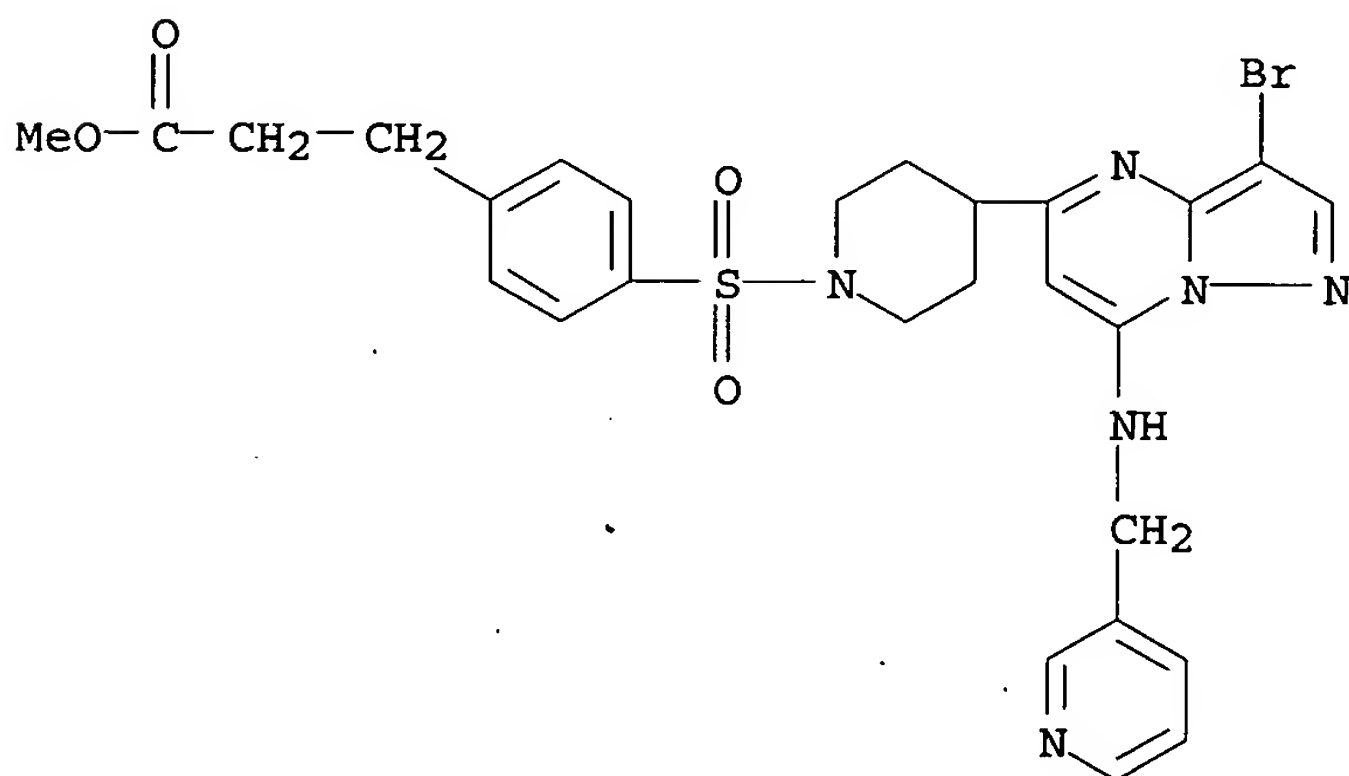


RN 677793-57-6 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



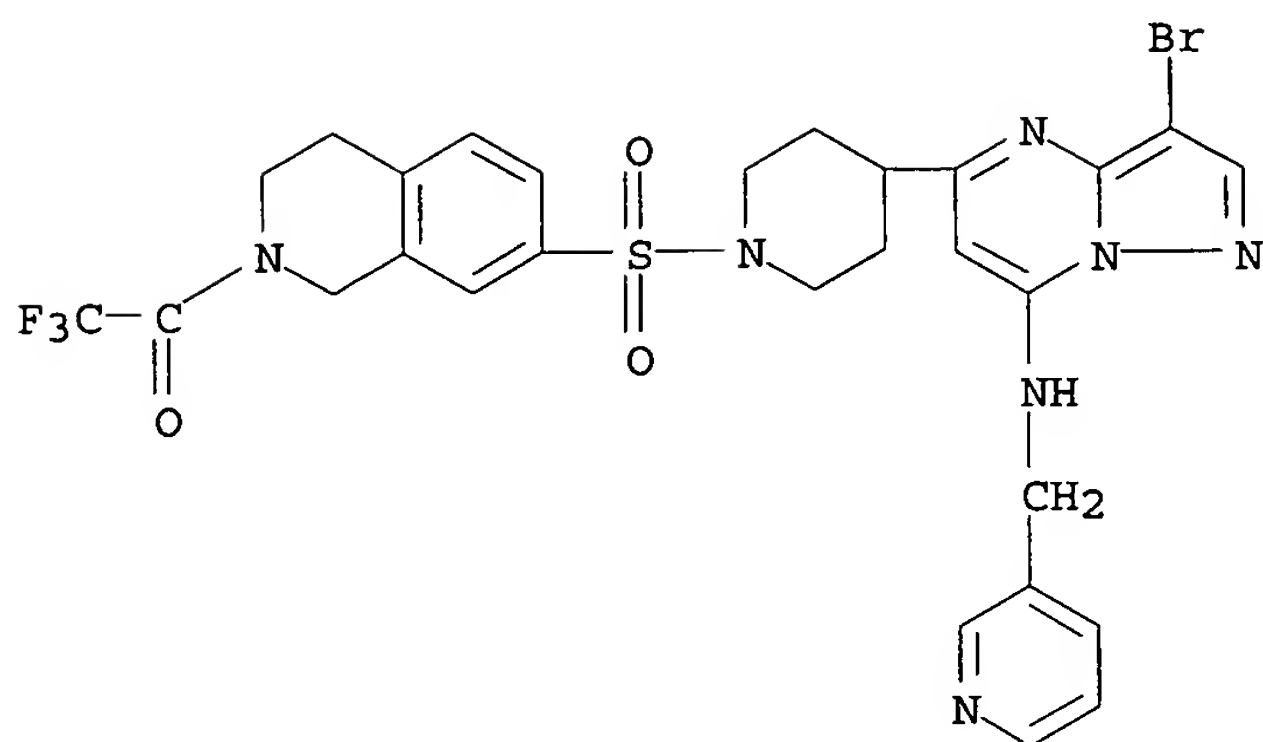
RN 677793-58-7 HCAPLUS

CN Benzenepropanoic acid, 4-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

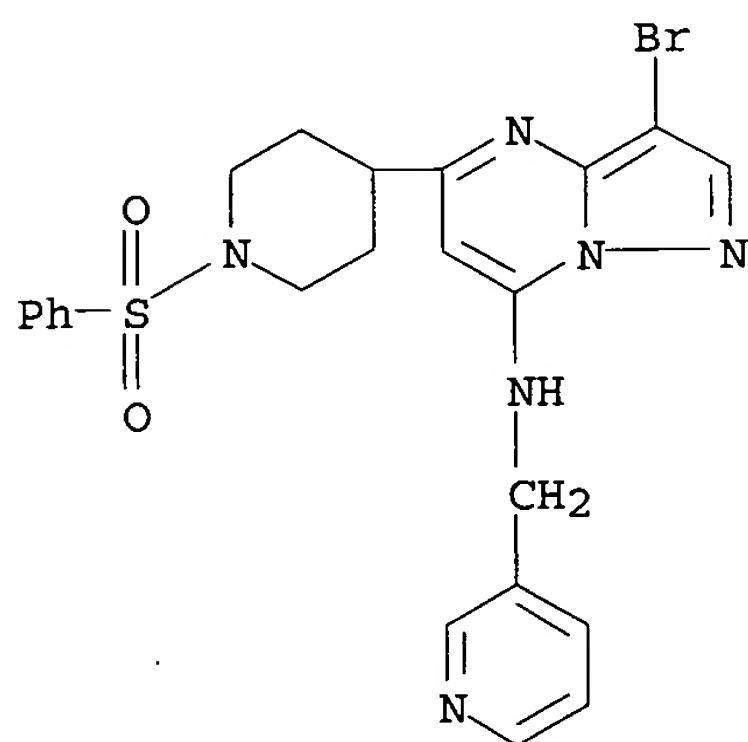


RN 677793-59-8 HCAPLUS

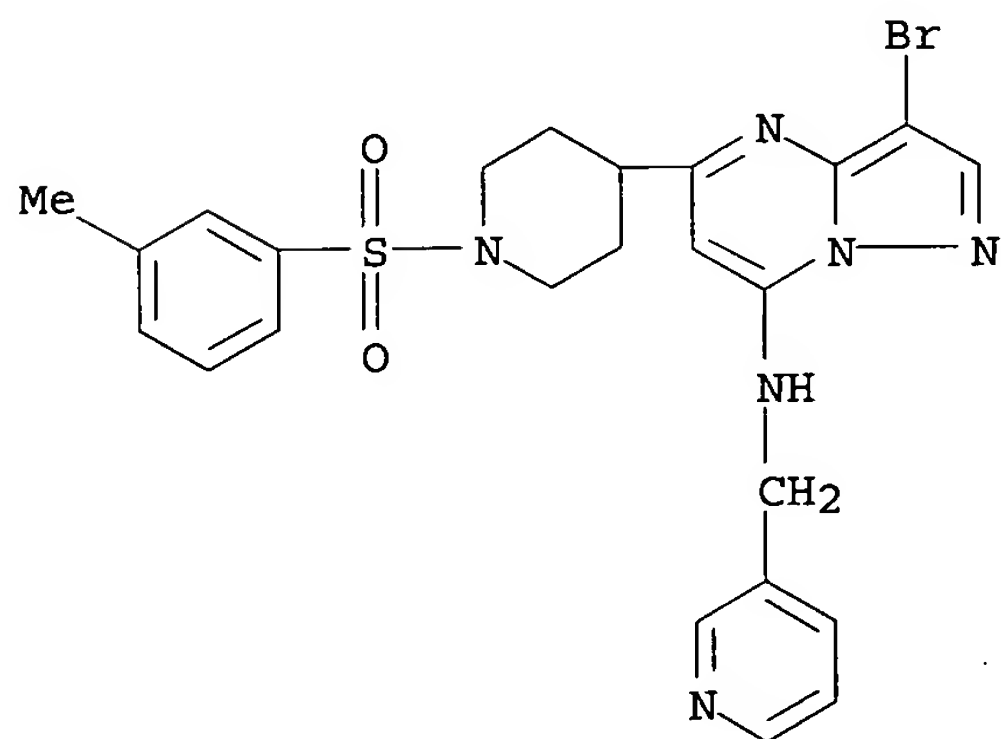
CN Isoquinoline, 7-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-1,2,3,4-tetrahydro-2-(trifluoroacetyl)- (9CI) (CA INDEX NAME)



RN 677793-60-1 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

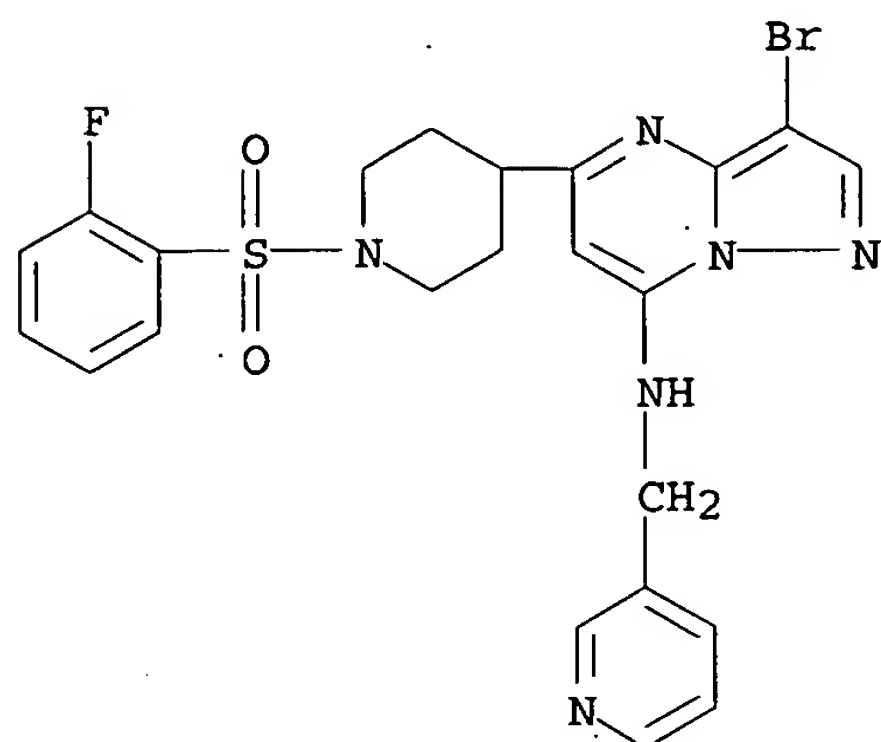


RN 677793-61-2 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



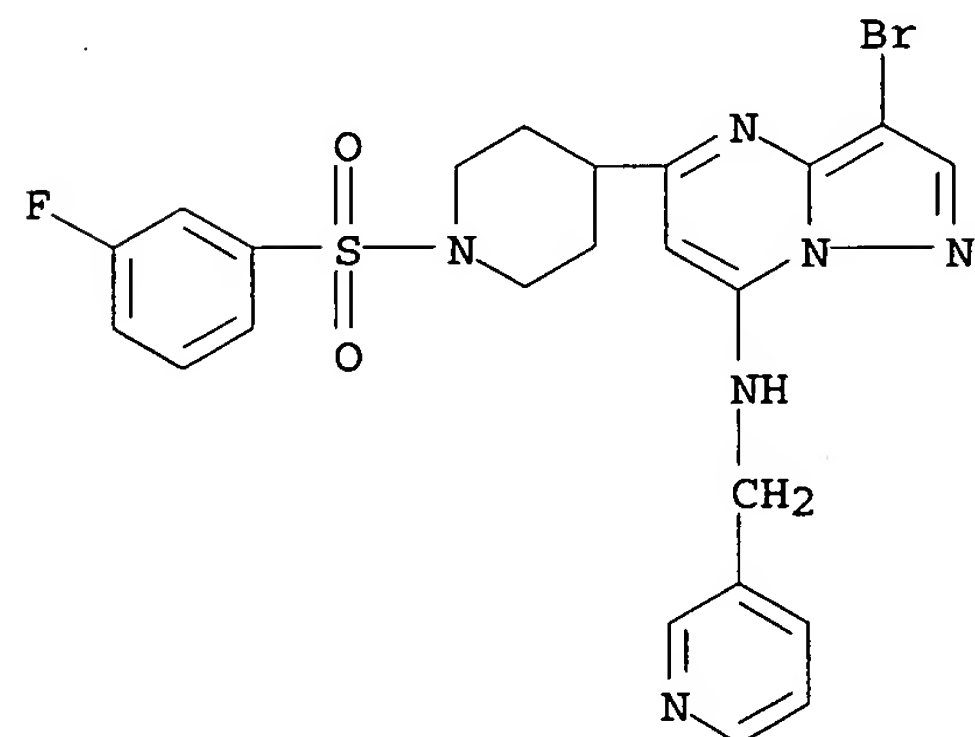
RN 677793-62-3 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



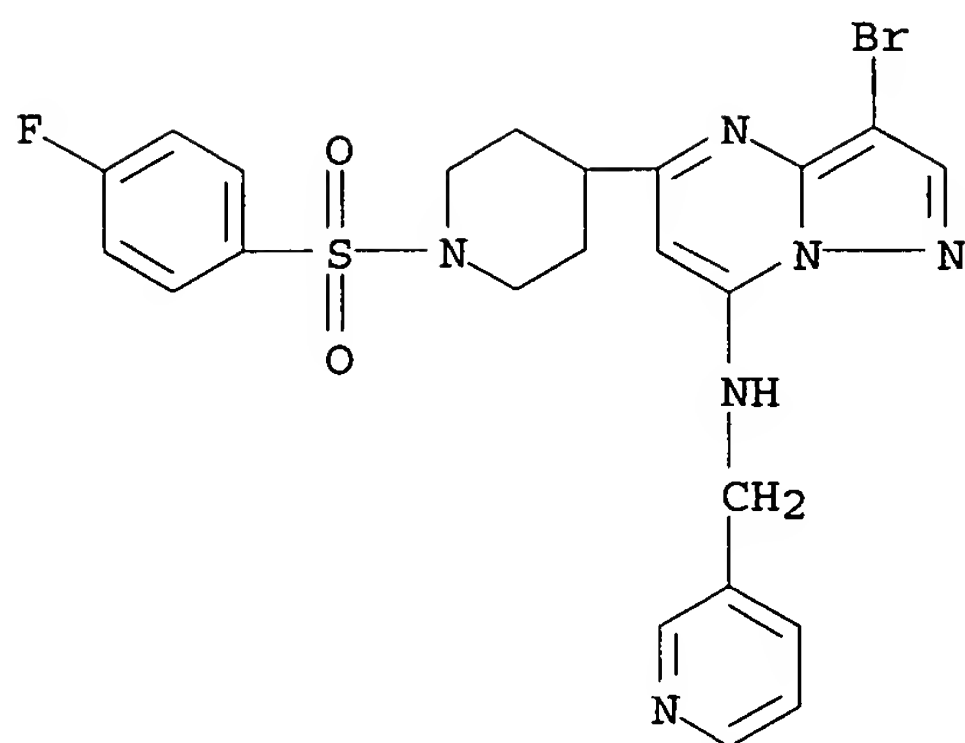
RN 677793-63-4 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

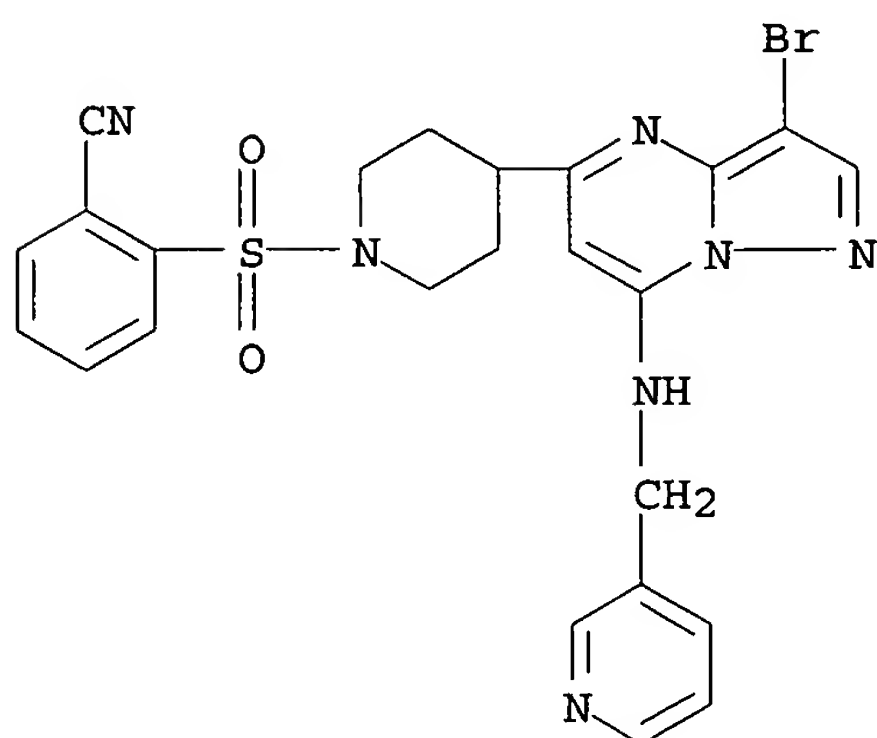


RN 677793-64-5 HCAPLUS

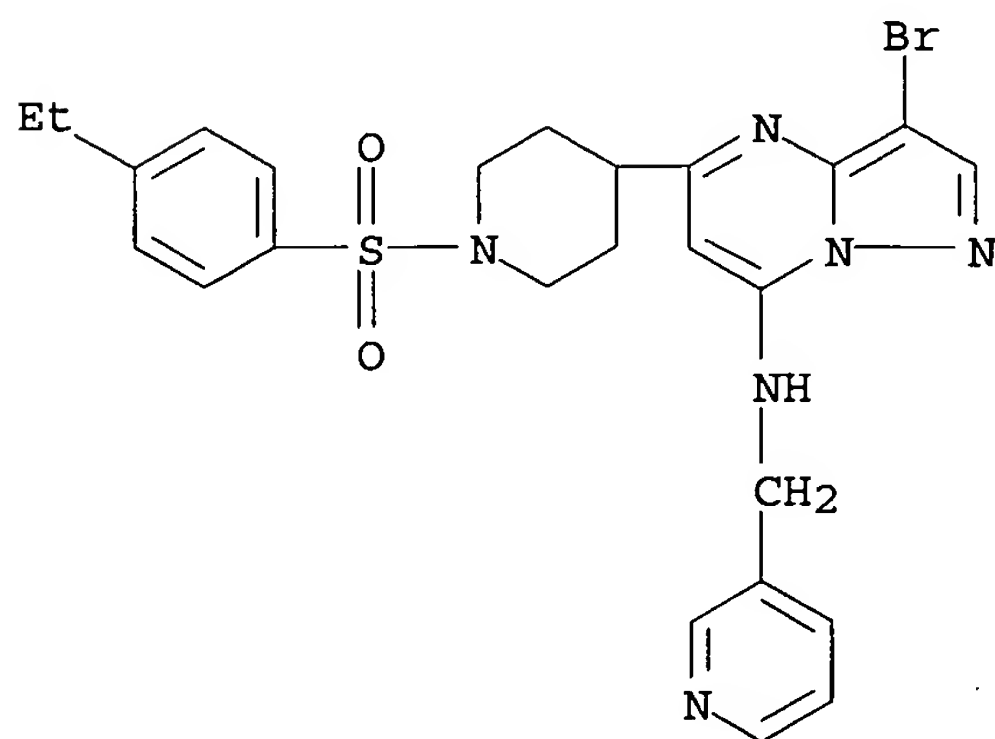
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677793-65-6 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

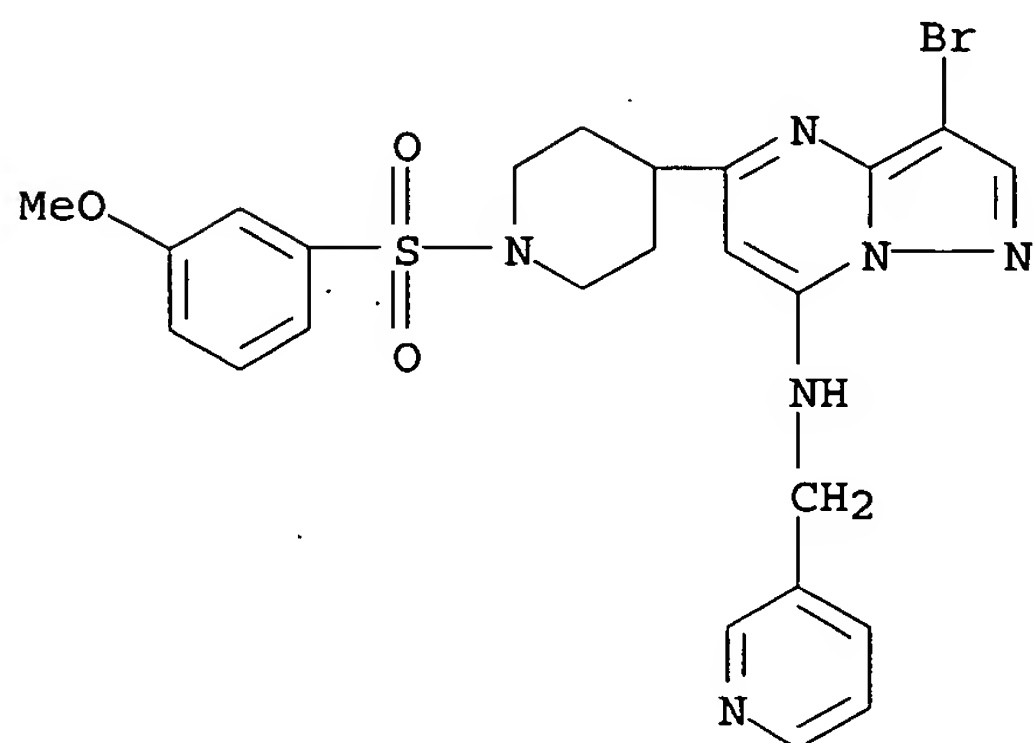


RN 677793-66-7 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-ethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



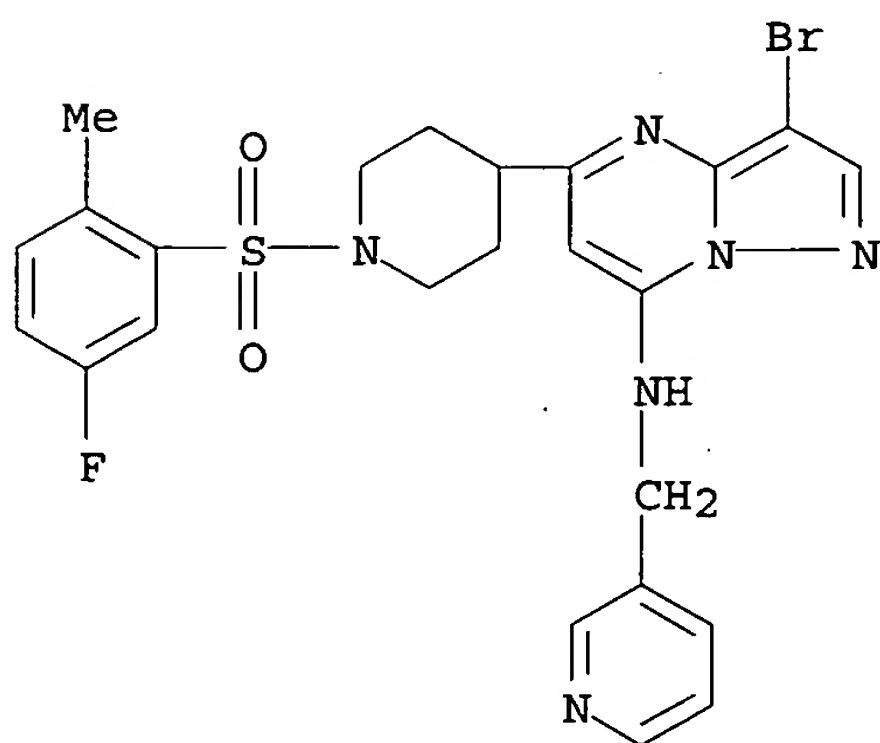
RN 677793-67-8 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



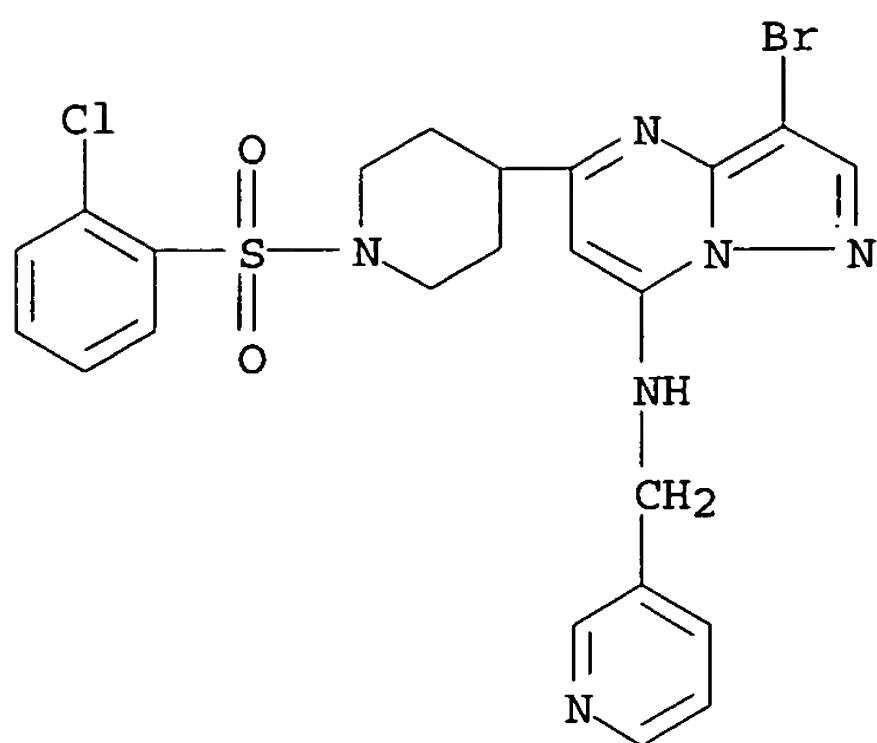
RN 677793-68-9 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-fluoro-2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

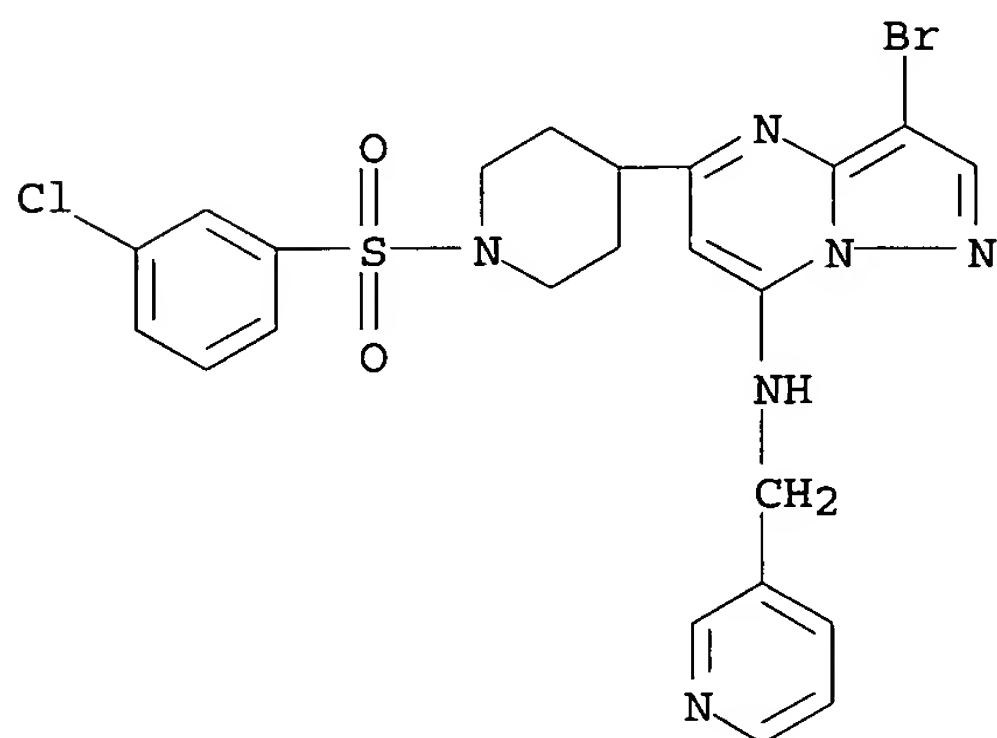


RN 677793-69-0 HCAPLUS

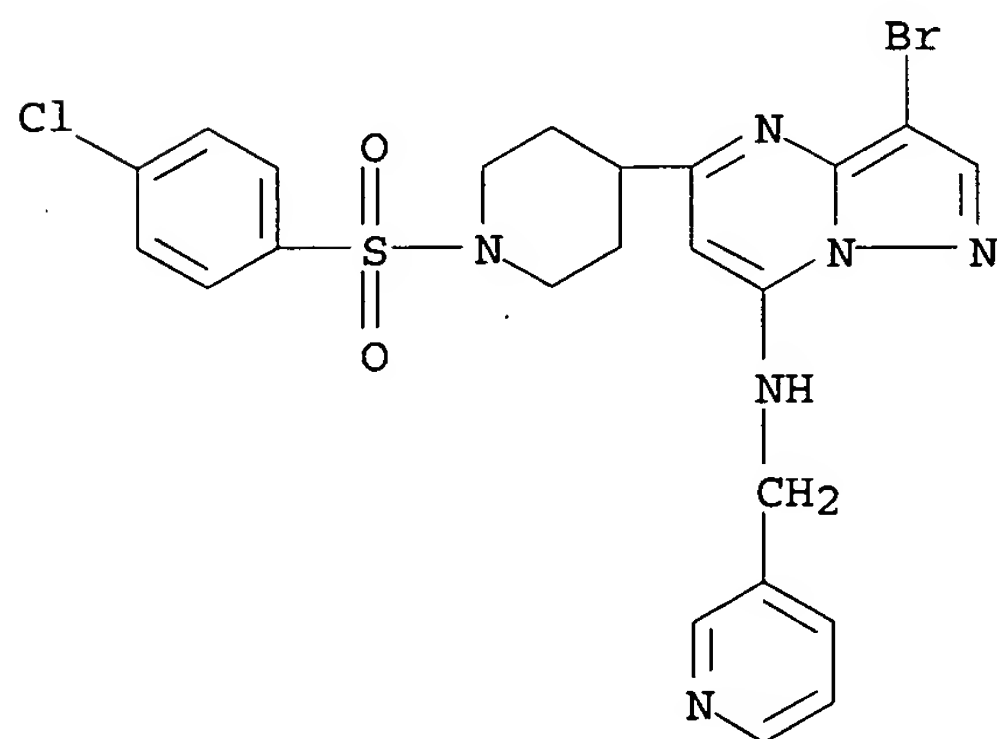
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677793-70-3 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-  
 alpyrimidin-5-yl]-1-[(3-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



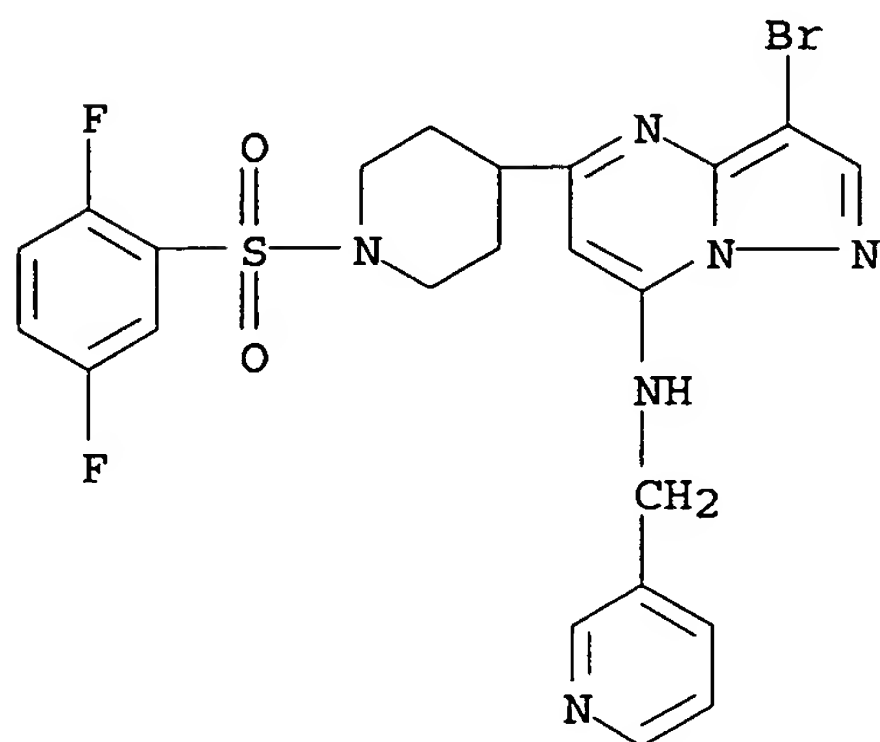
RN 677793-71-4 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-  
 alpyrimidin-5-yl]-1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677793-72-5 HCAPLUS

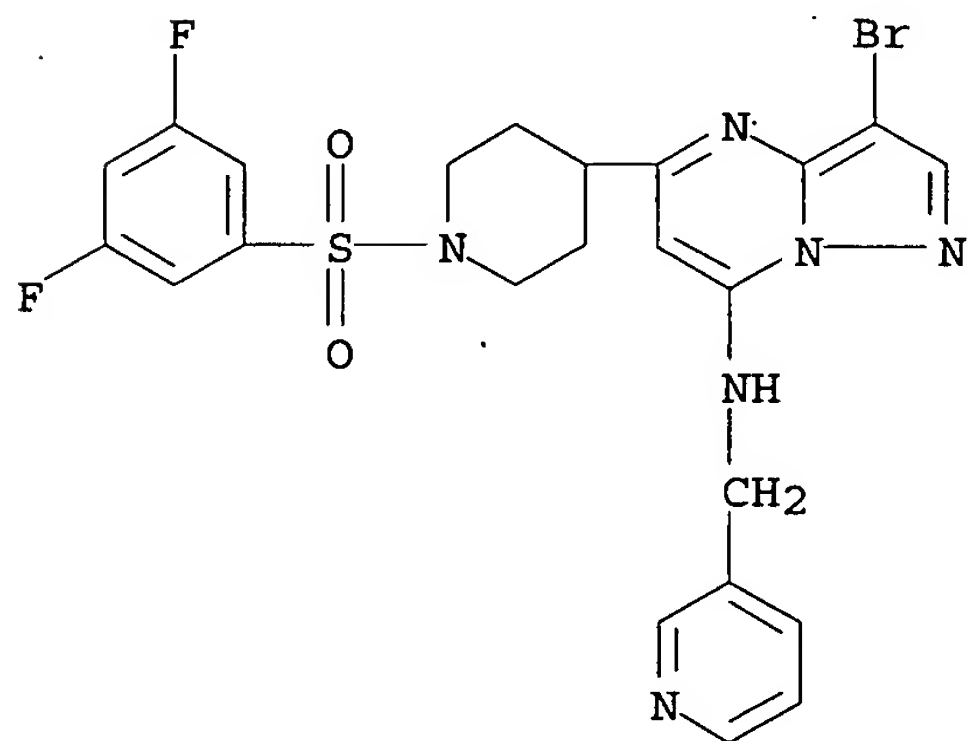


CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



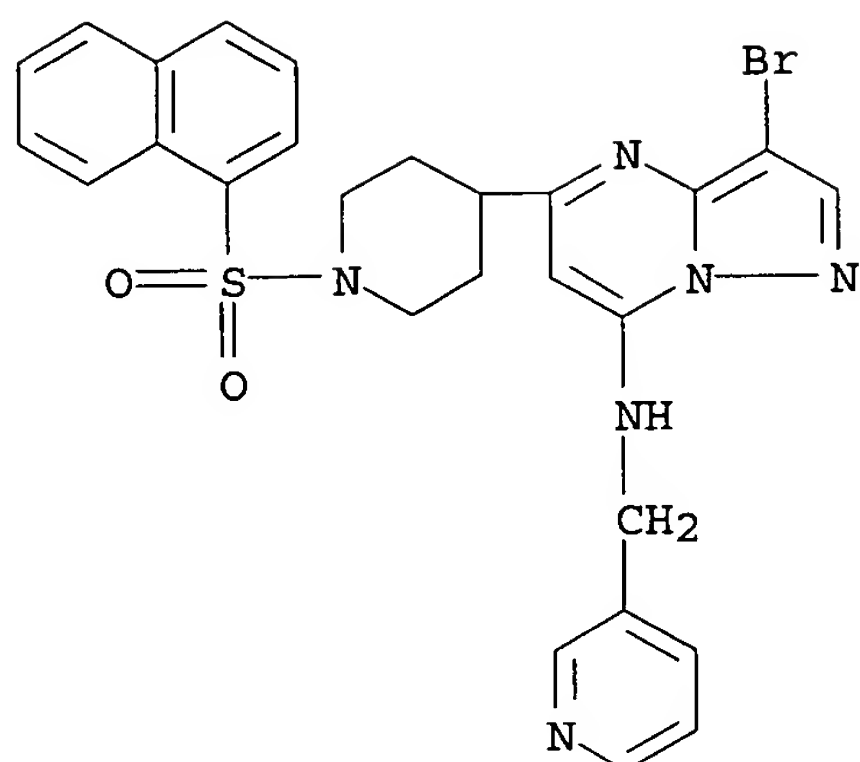
RN 677793-73-6 HCAPLUS

CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

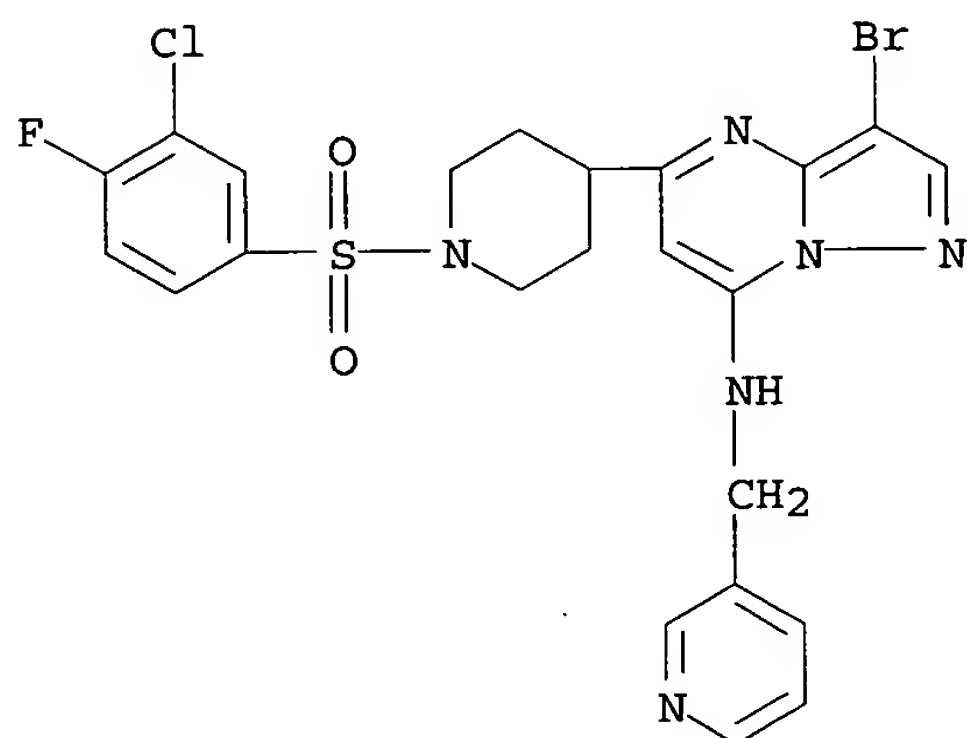


RN 677793-74-7 HCAPLUS

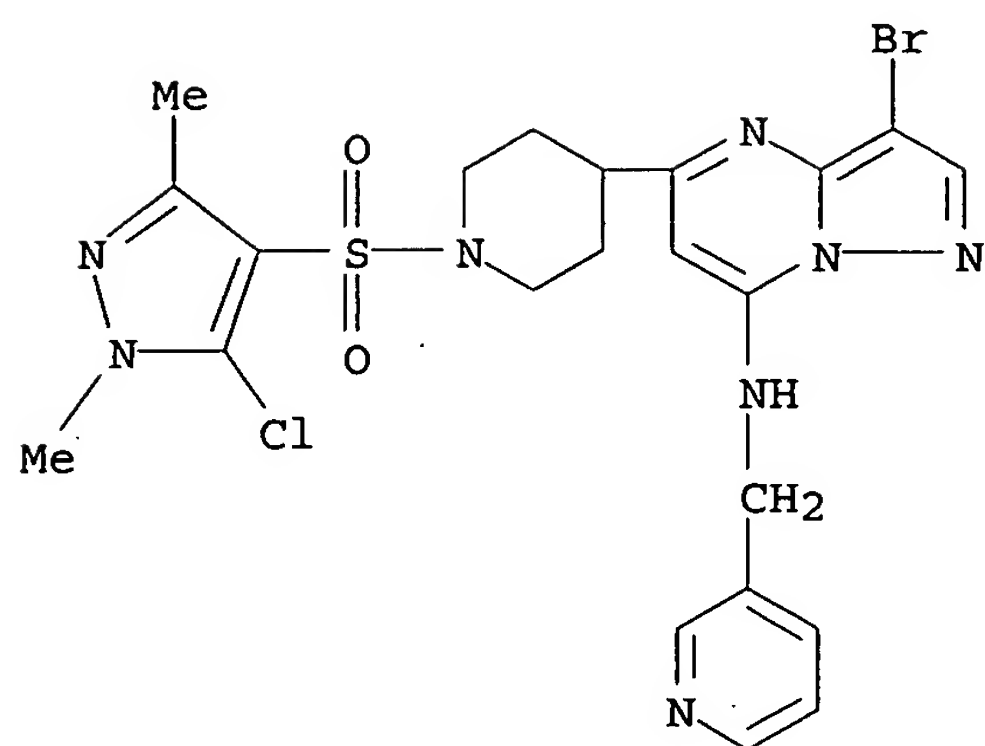
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



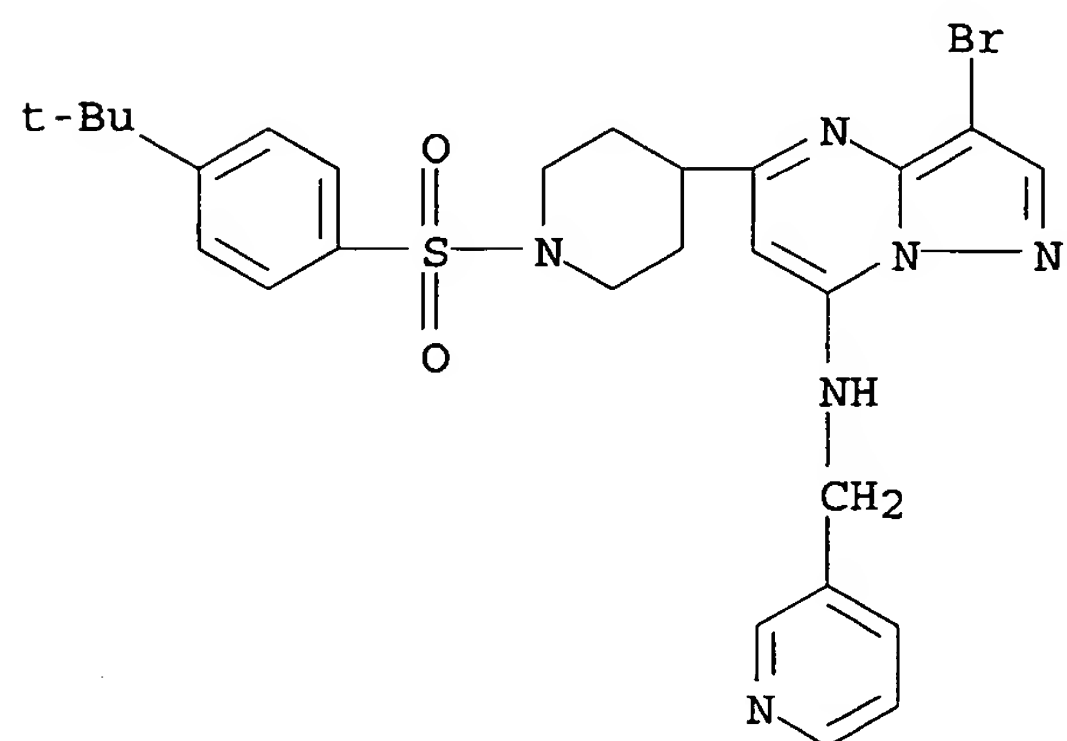
RN 677793-75-8 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



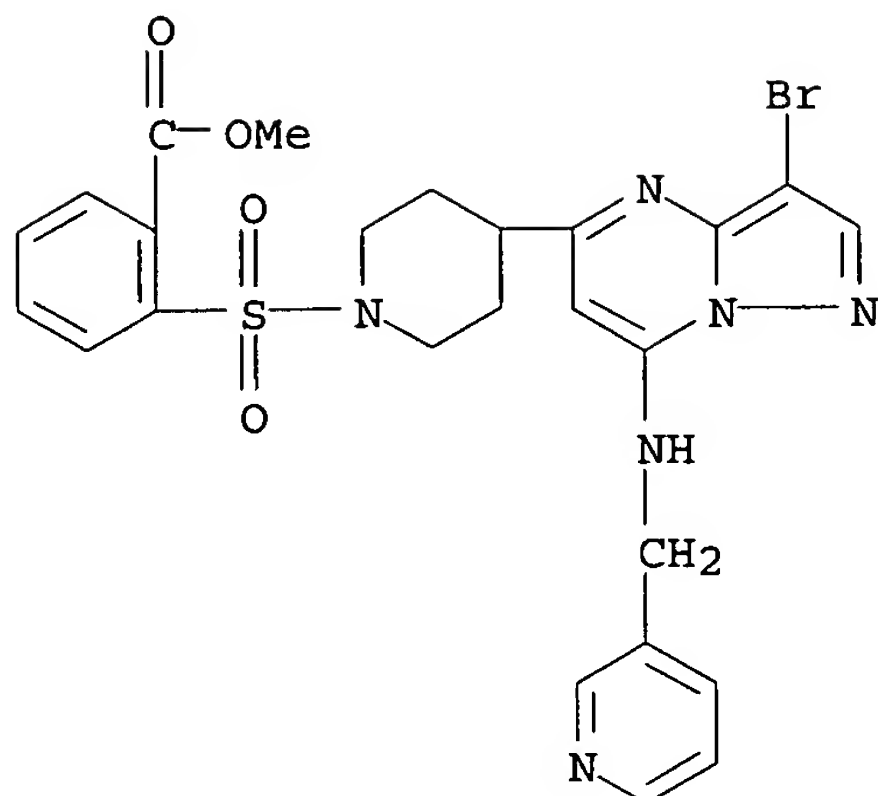
RN 677793-76-9 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]- (9CI) (CA INDEX NAME)



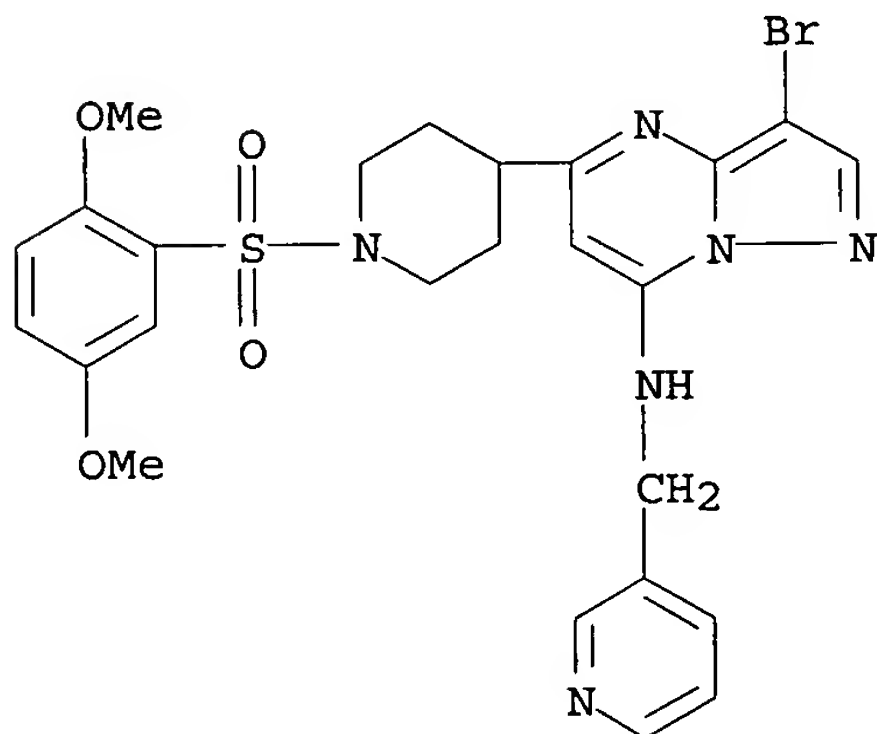
RN 677793-77-0 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



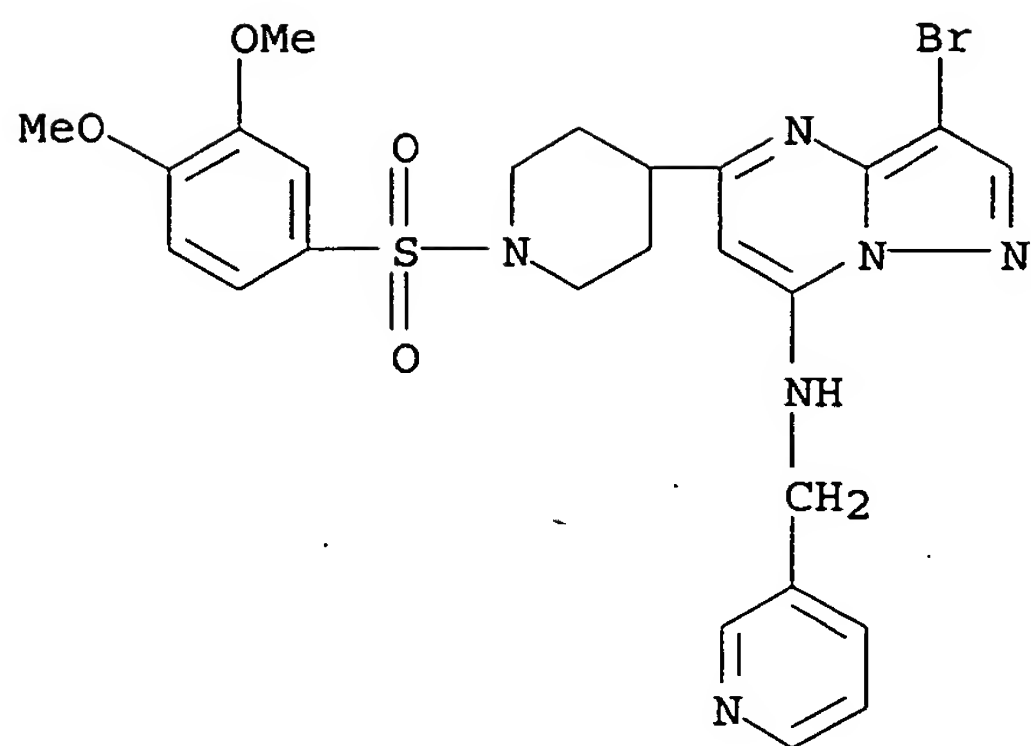
RN 677793-78-1 HCAPLUS  
 CN Benzoic acid, 2-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 677793-79-2 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

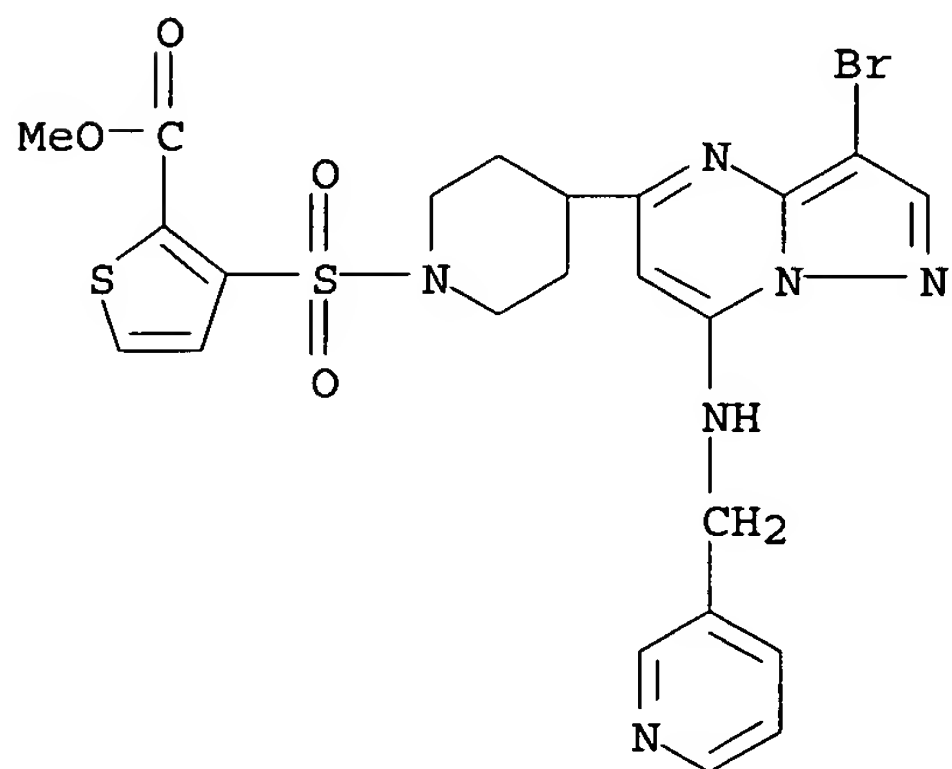


RN 677793-80-5 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



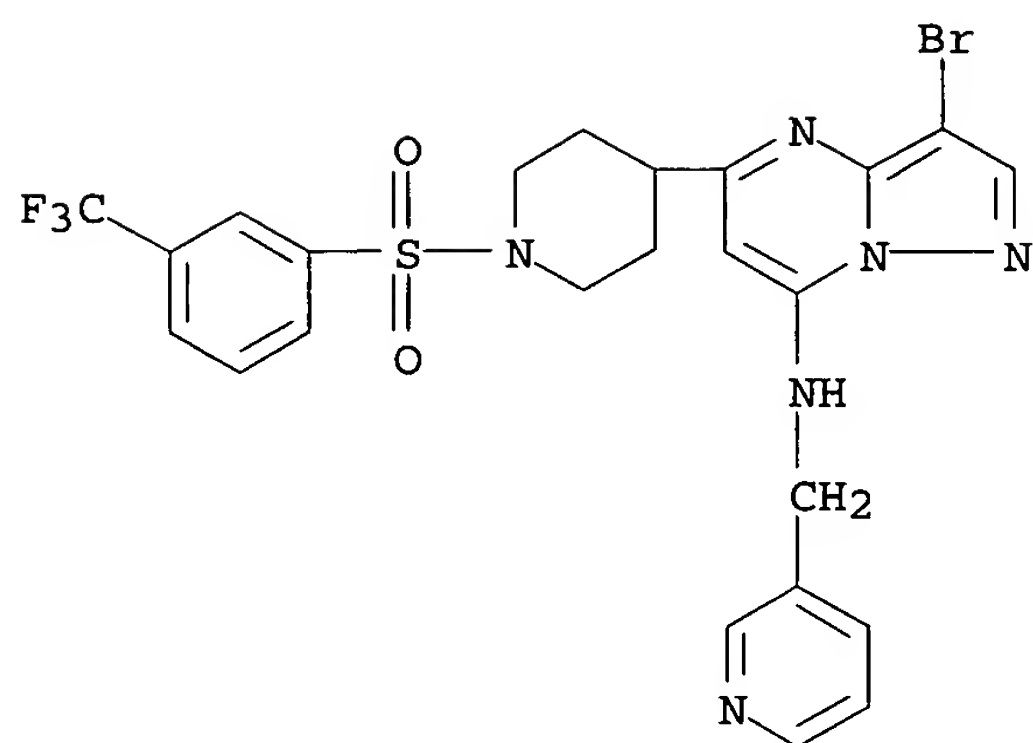
RN 677793-81-6 HCAPLUS

CN 2-Thiophenecarboxylic acid, 3-[[4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

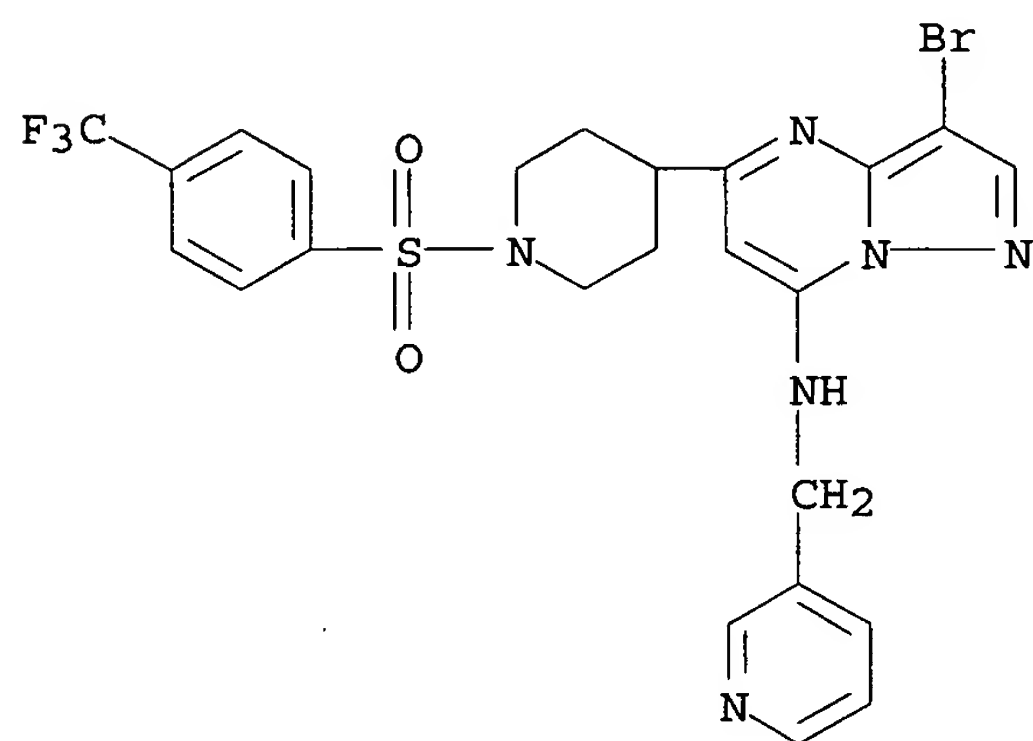


RN 677793-82-7 HCAPLUS

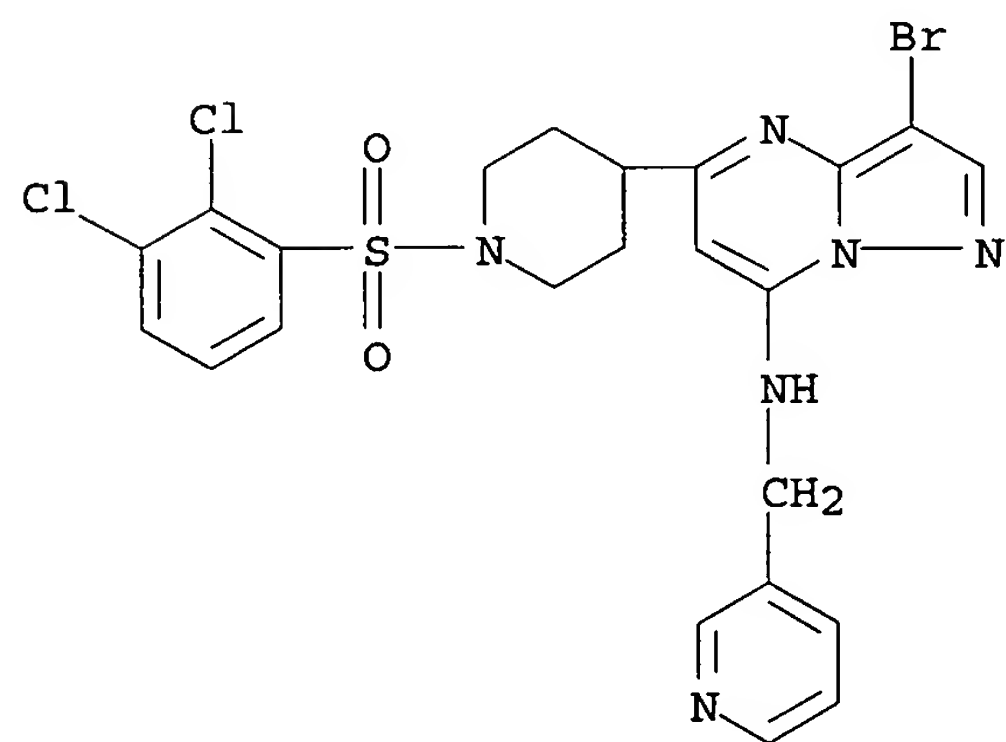
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



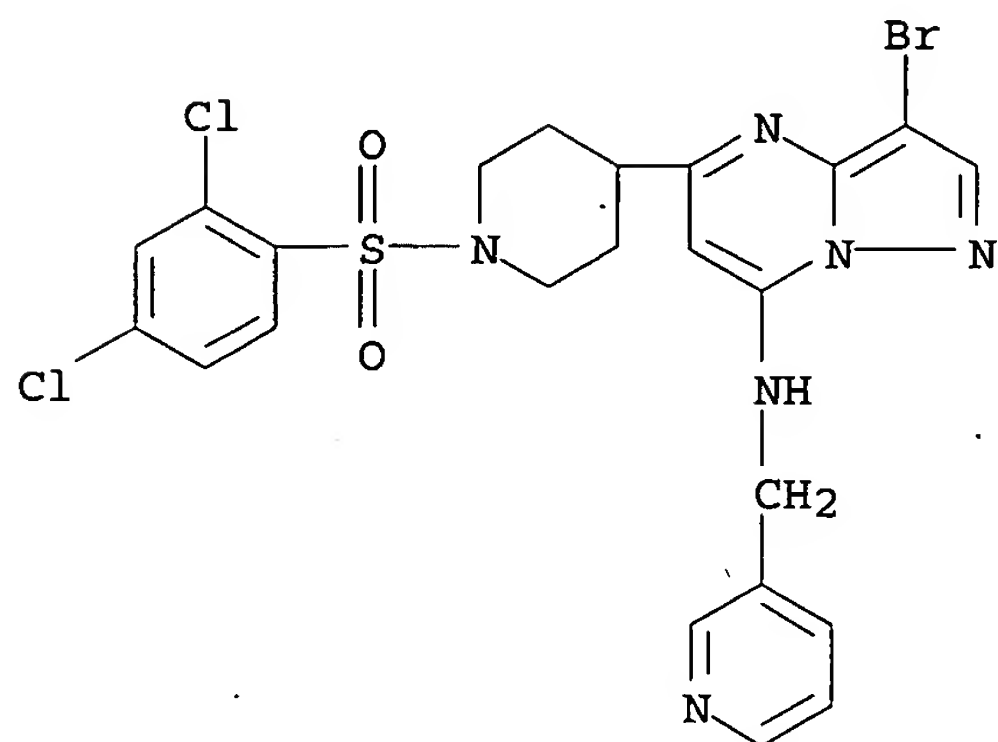
RN 677793-83-8 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



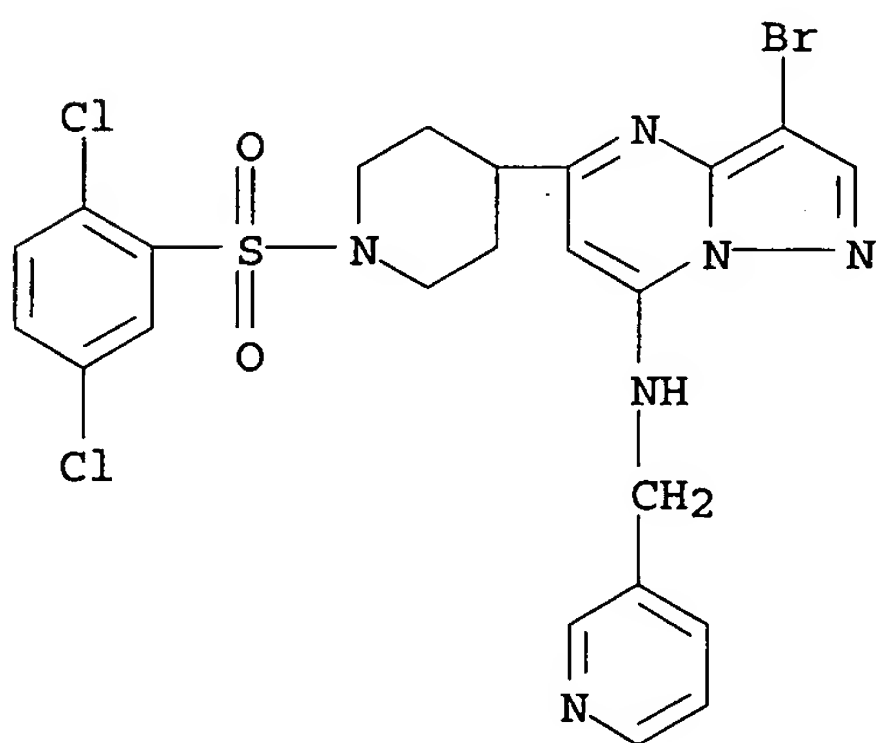
RN 677793-84-9 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2,3-dichlorophenyl]sulfonyl]- (9CI) (CA INDEX NAME)



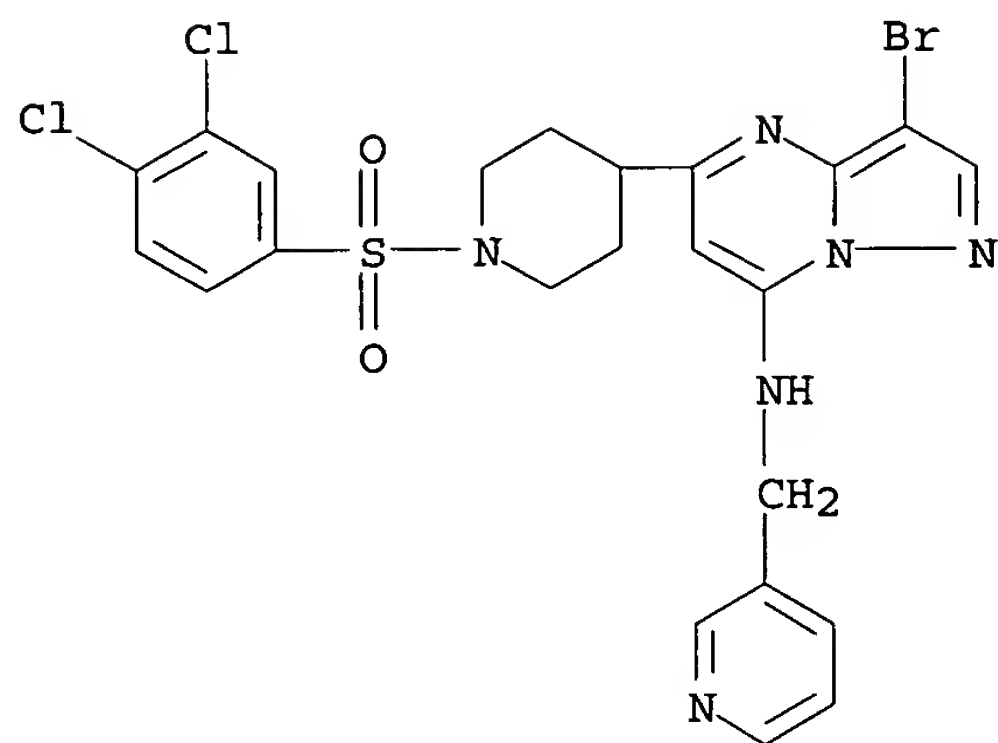
RN 677793-85-0 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



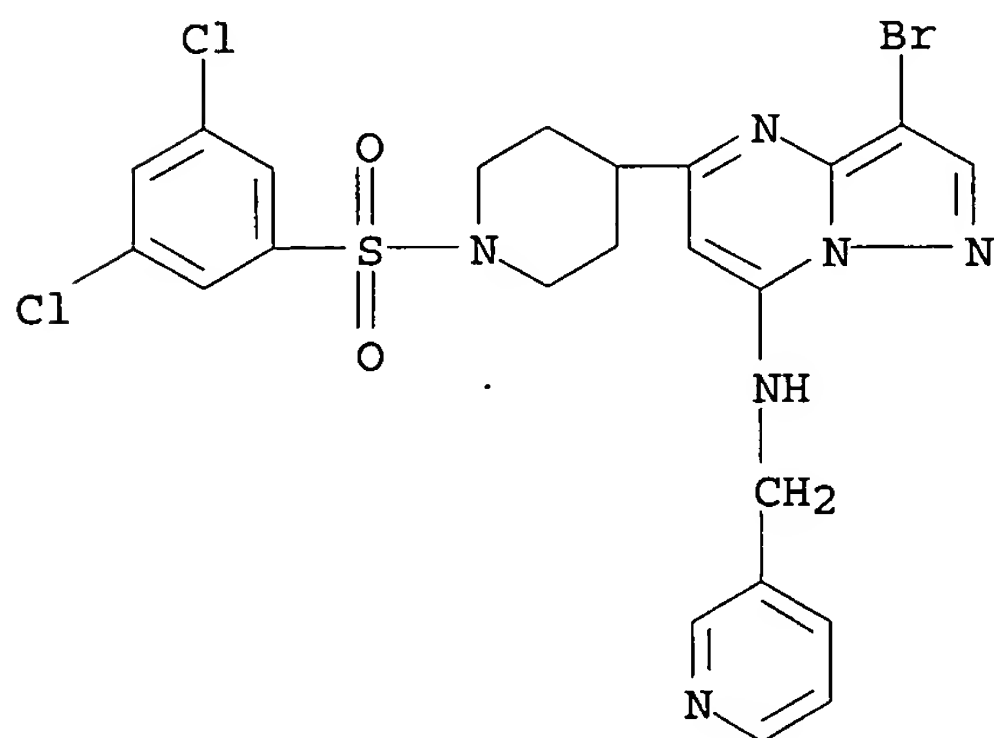
RN 677793-86-1 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



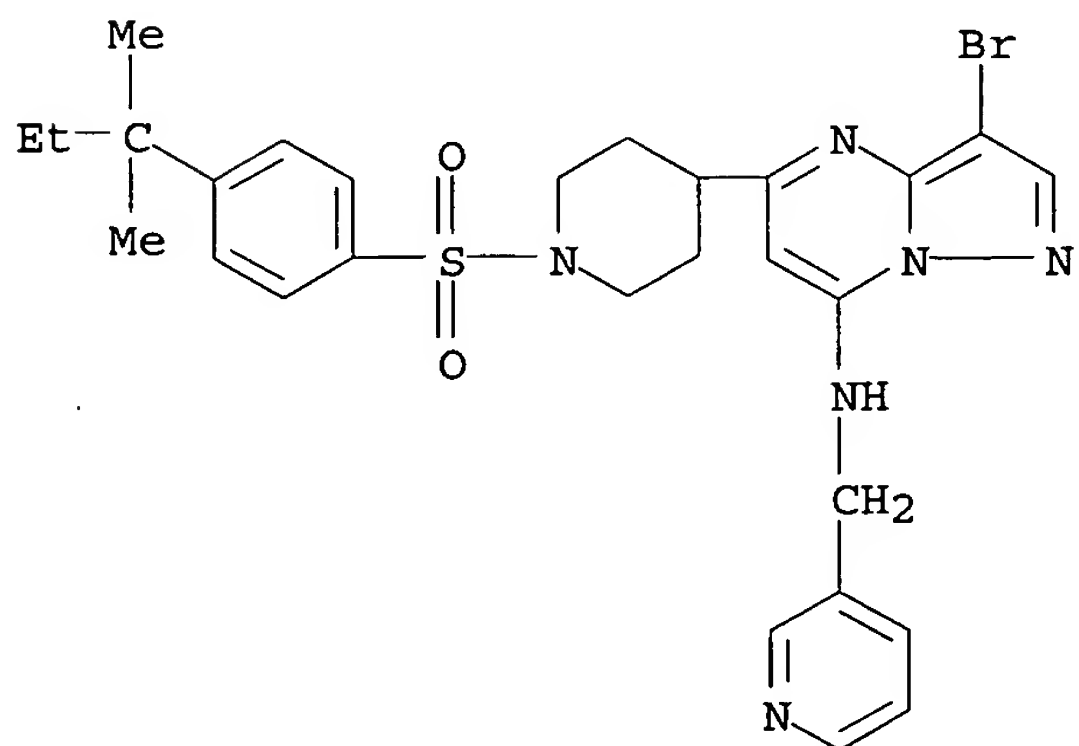
RN 677793-87-2 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677793-88-3 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

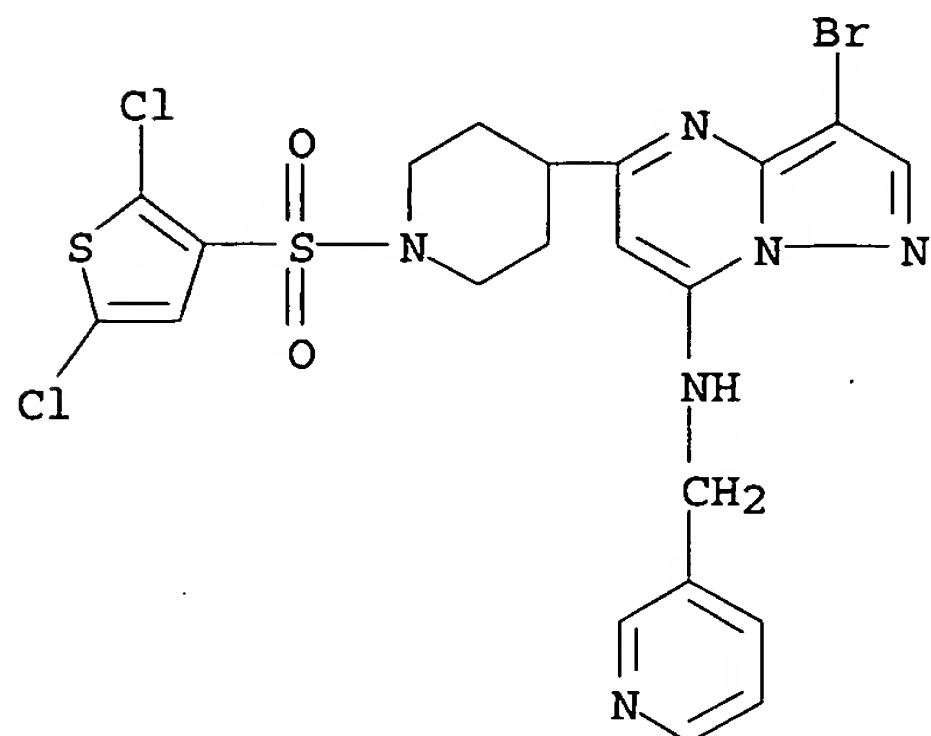


RN 677793-89-4 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylpropyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

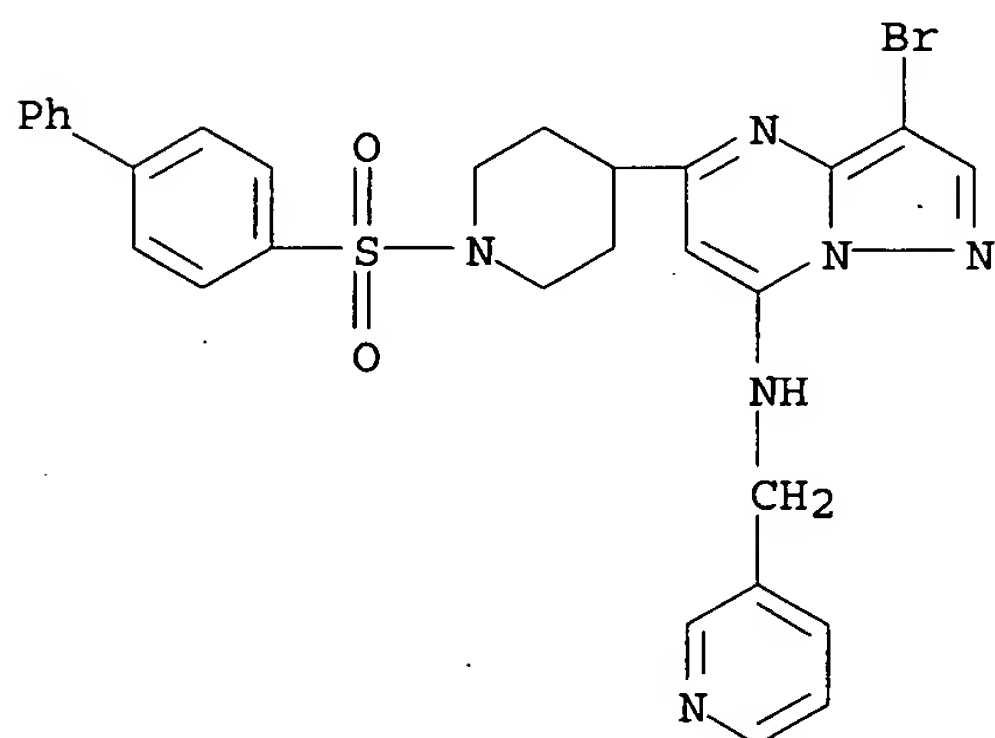




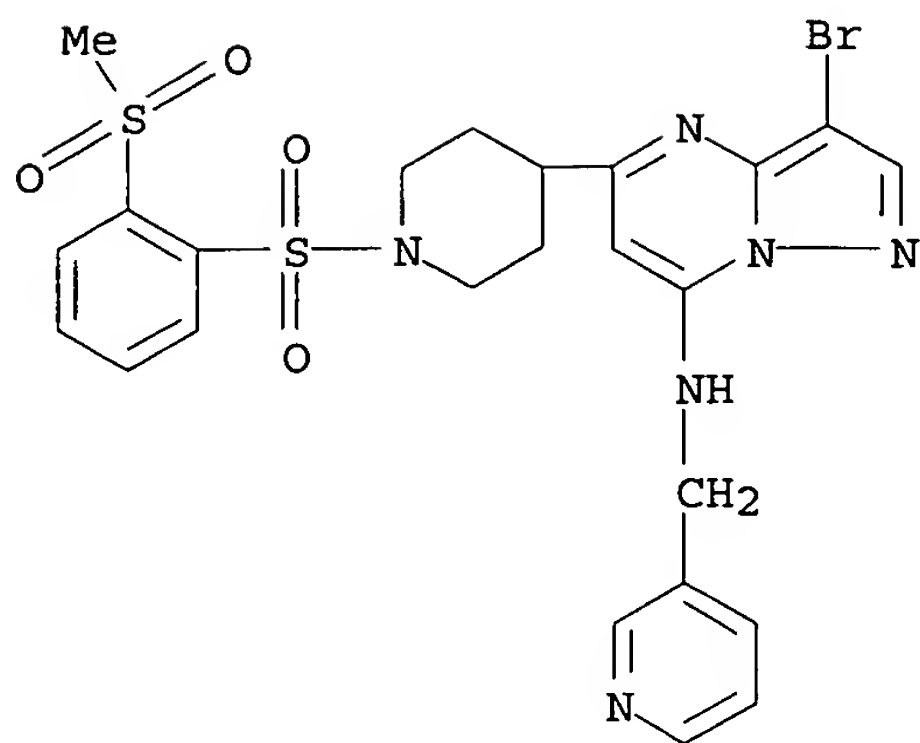
RN 677793-90-7 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dichloro-3-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)



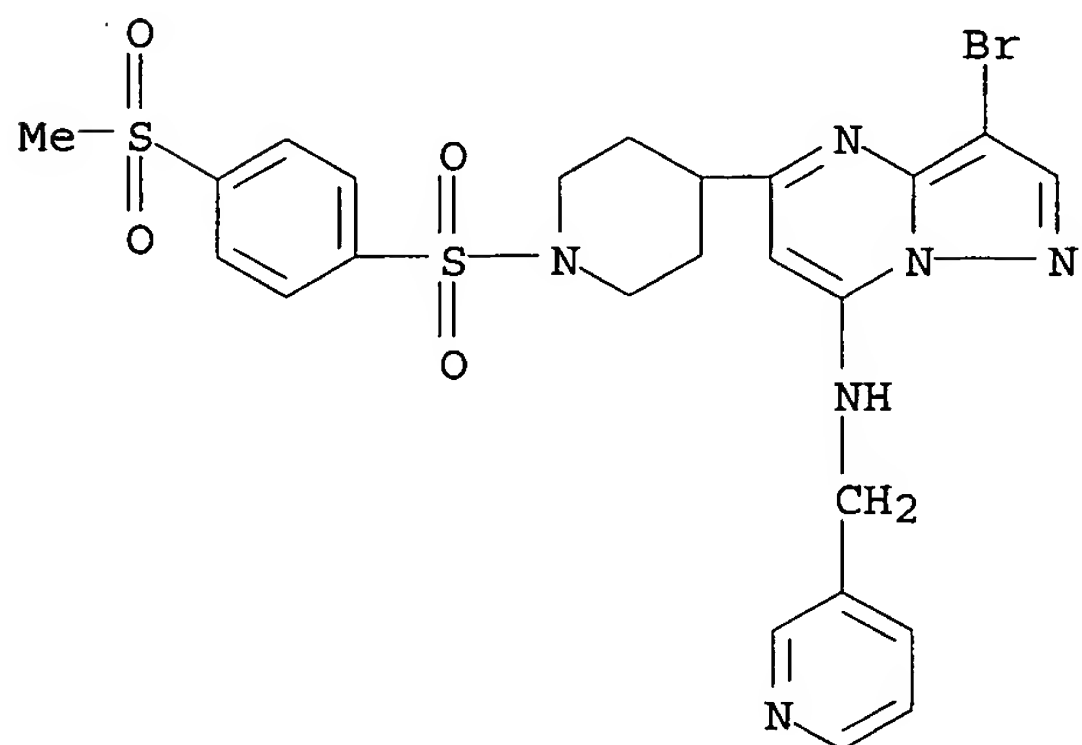
RN 677793-91-8 HCAPLUS  
 CN Piperidine, 1-([1,1'-biphenyl]-4-ylsulfonyl)-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



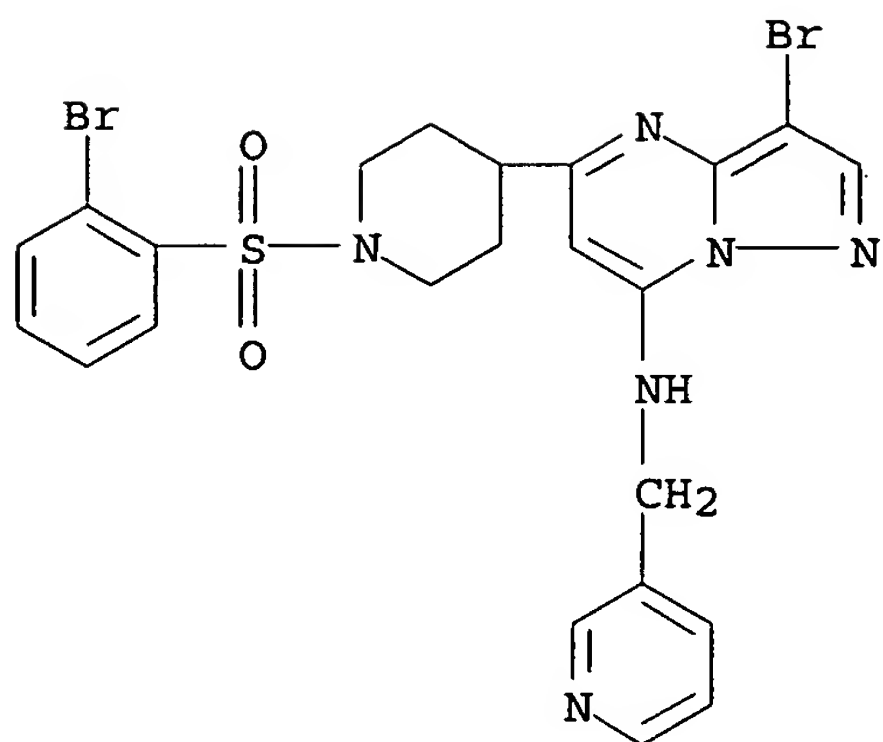
RN 677793-92-9 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 677793-93-0 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

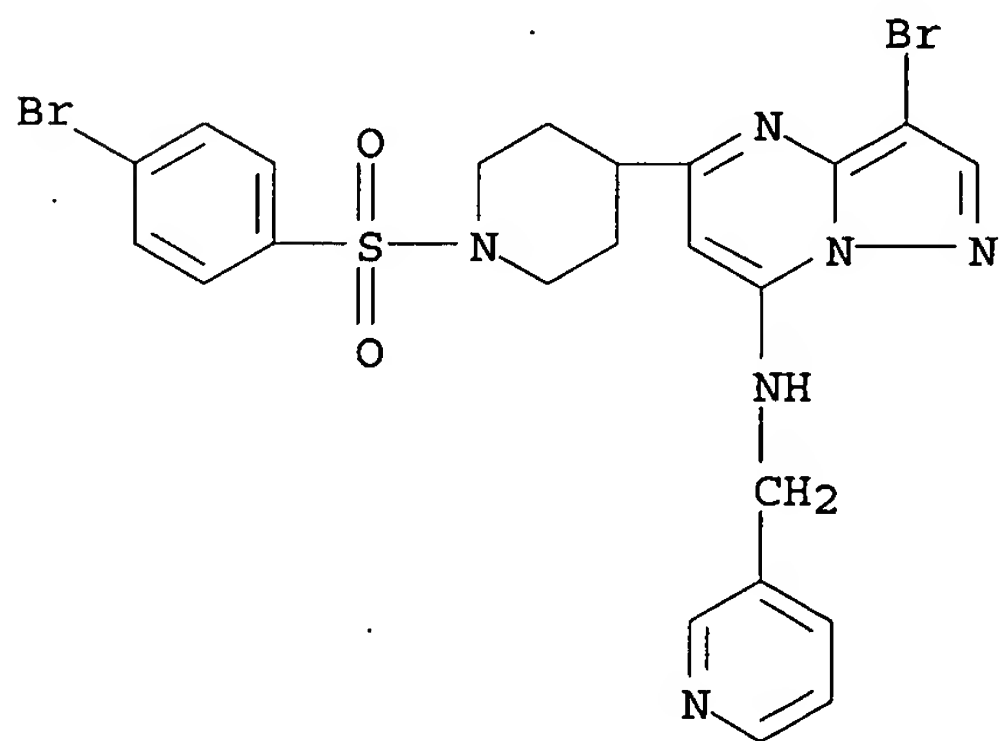


RN 677793-94-1 HCAPLUS  
 CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



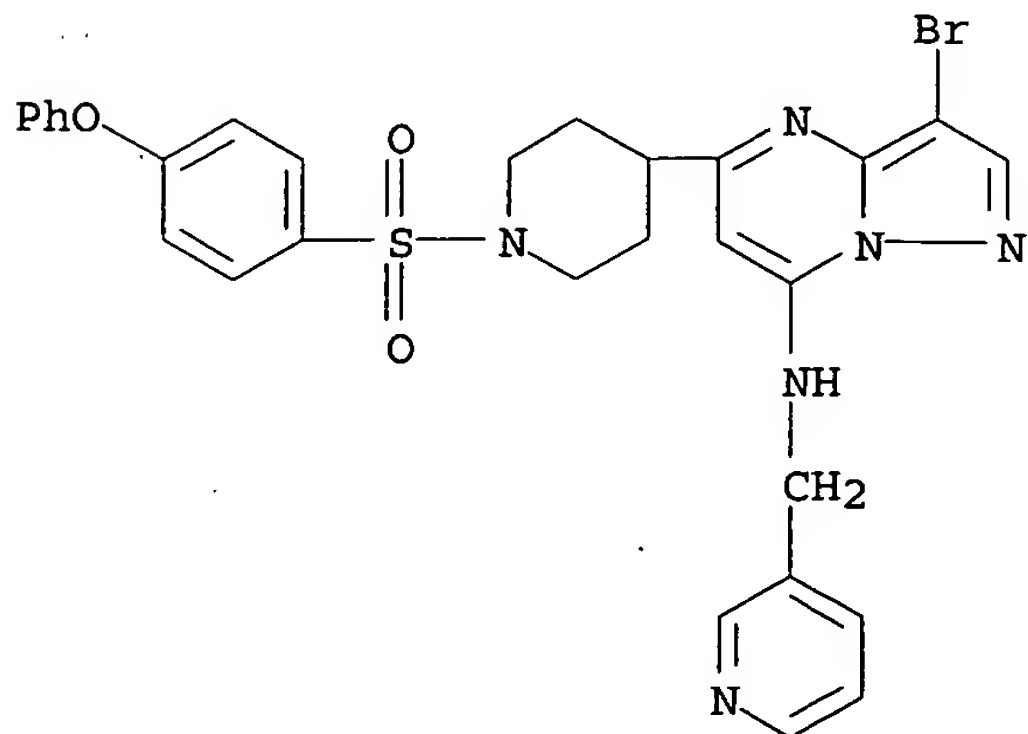
RN 677793-95-2 HCAPLUS

CN Piperidine, 1-[(4-bromophenyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

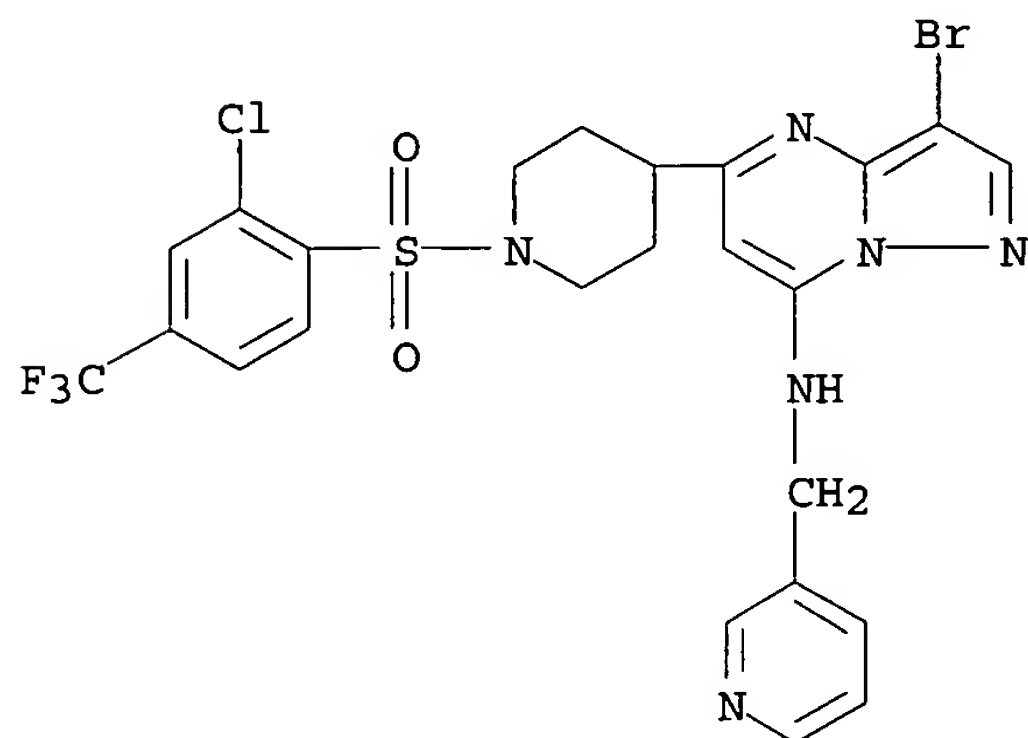


RN 677793-96-3 HCAPLUS

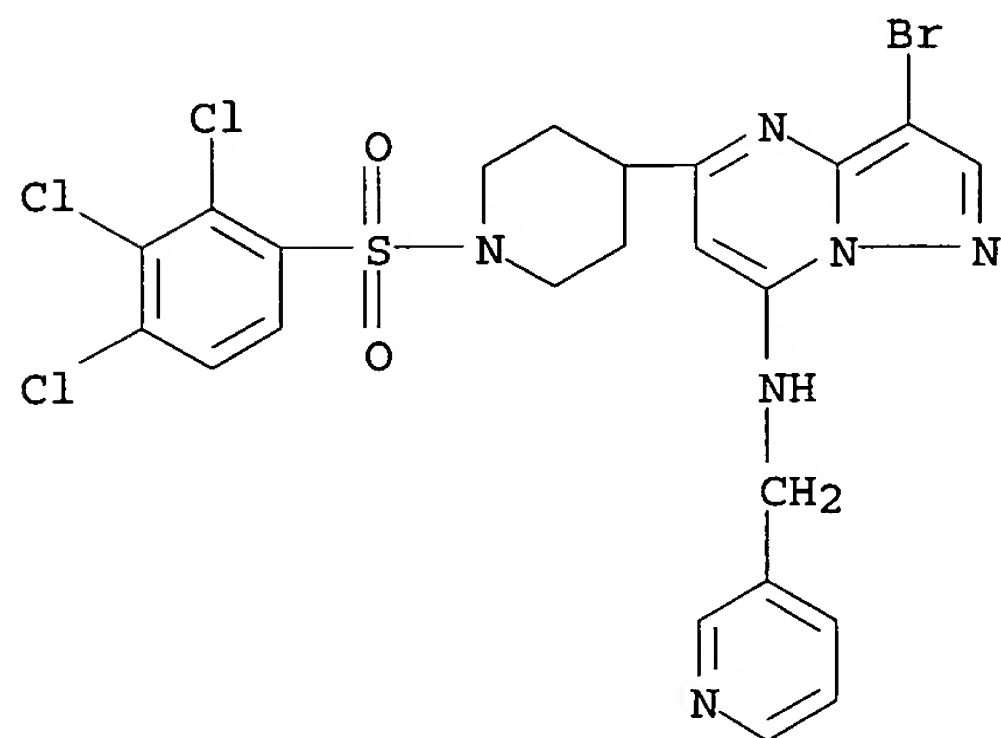
CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-phenoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



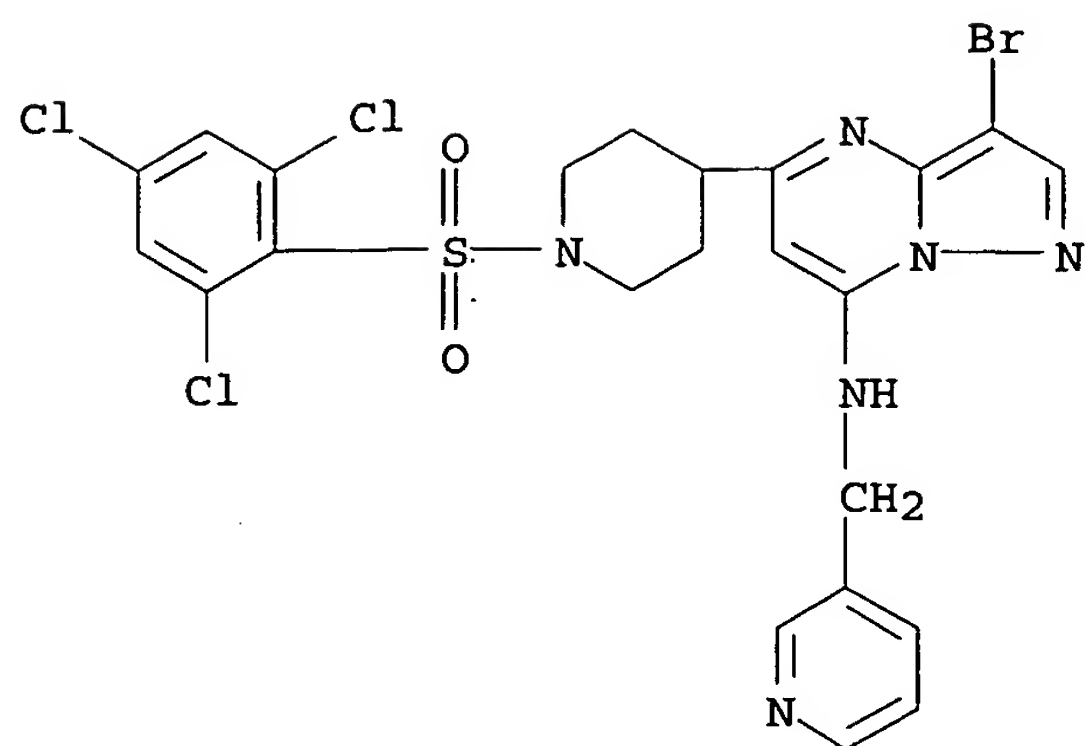
RN 677793-97-4 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl]- (9CI)  
 (CA INDEX NAME)



RN 677793-98-5 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3,4-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

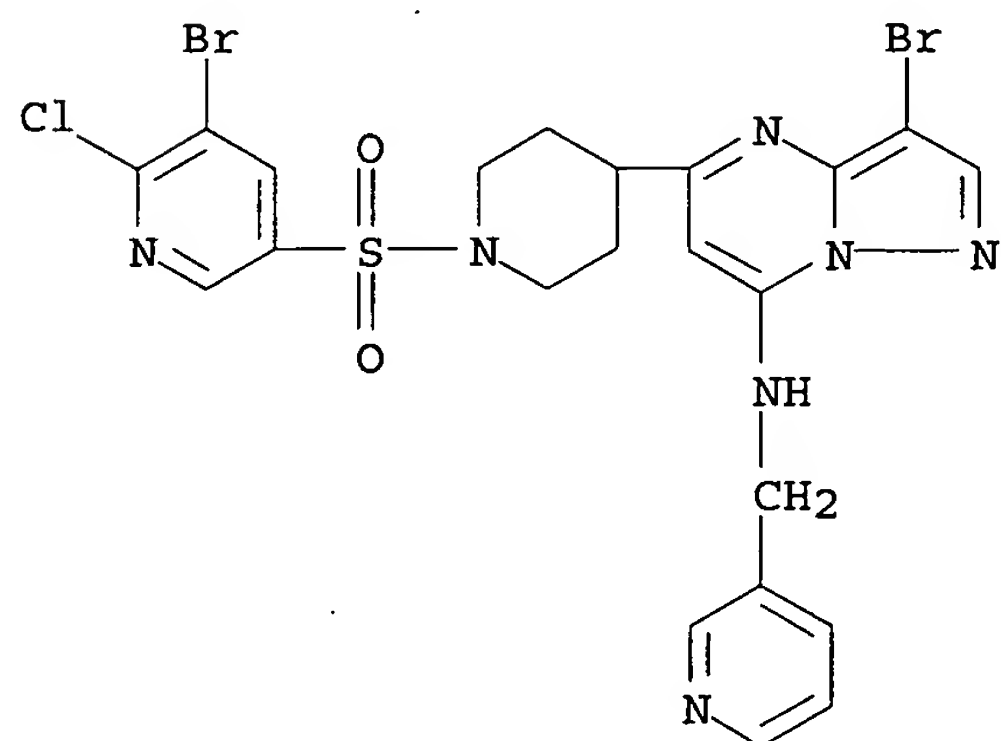


RN 677793-99-6 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



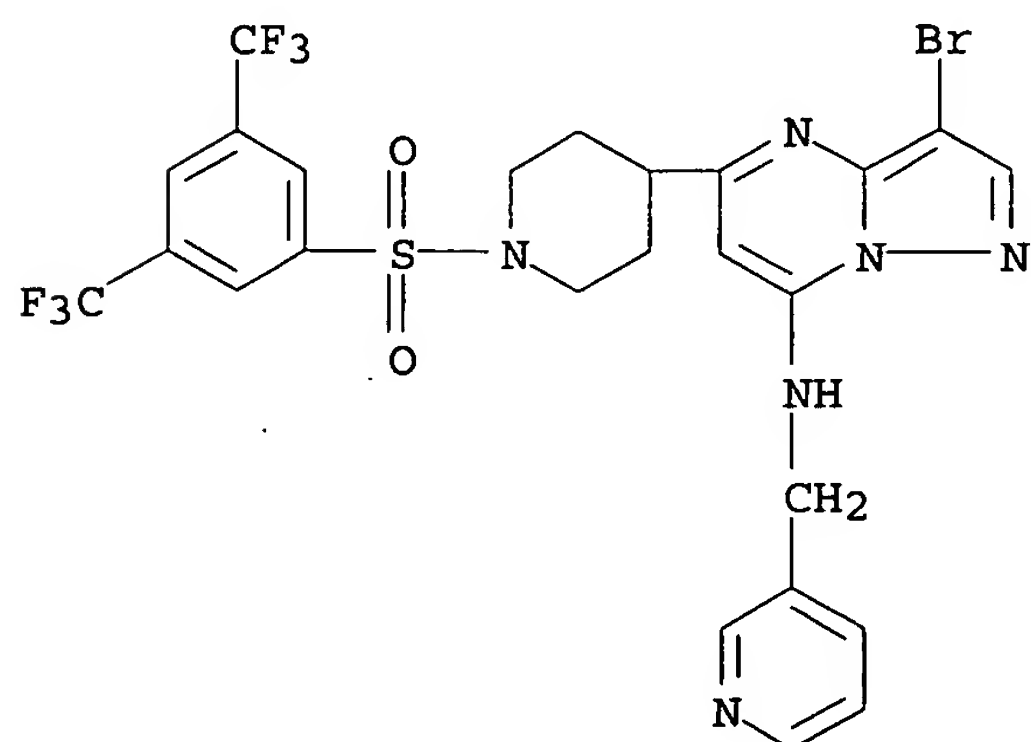
RN 677794-00-2 HCAPLUS

CN Piperidine, 1-[(5-bromo-6-chloro-3-pyridinyl)sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-(9CI) (CA INDEX NAME)

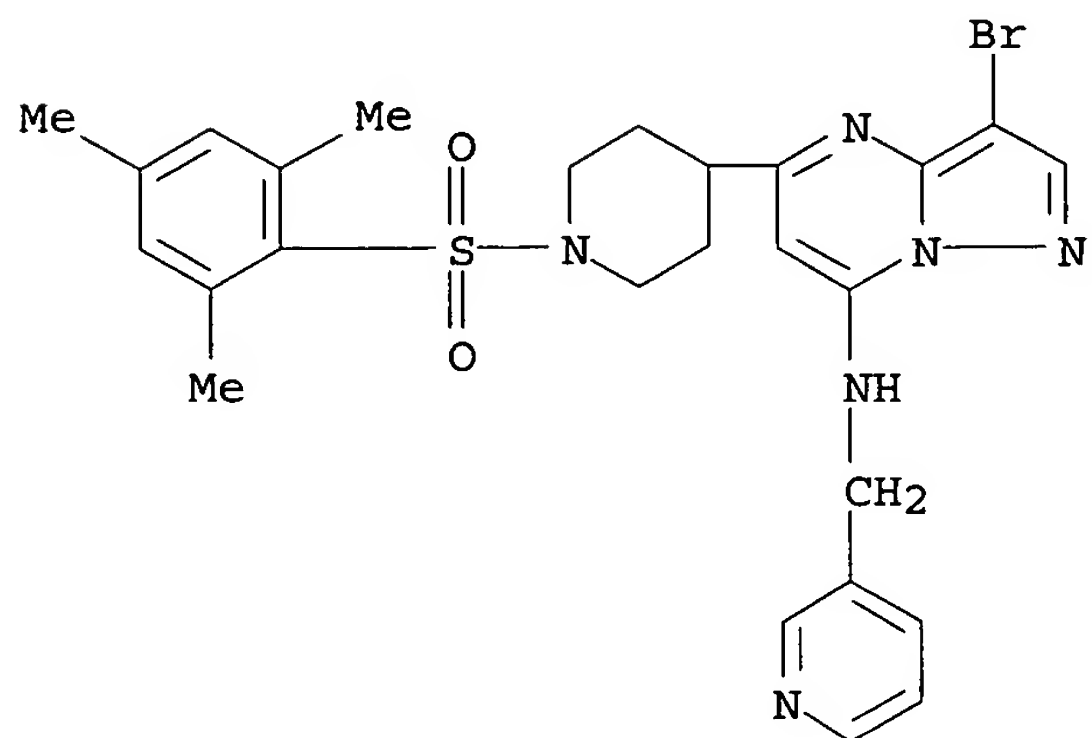


RN 677794-01-3 HCAPLUS

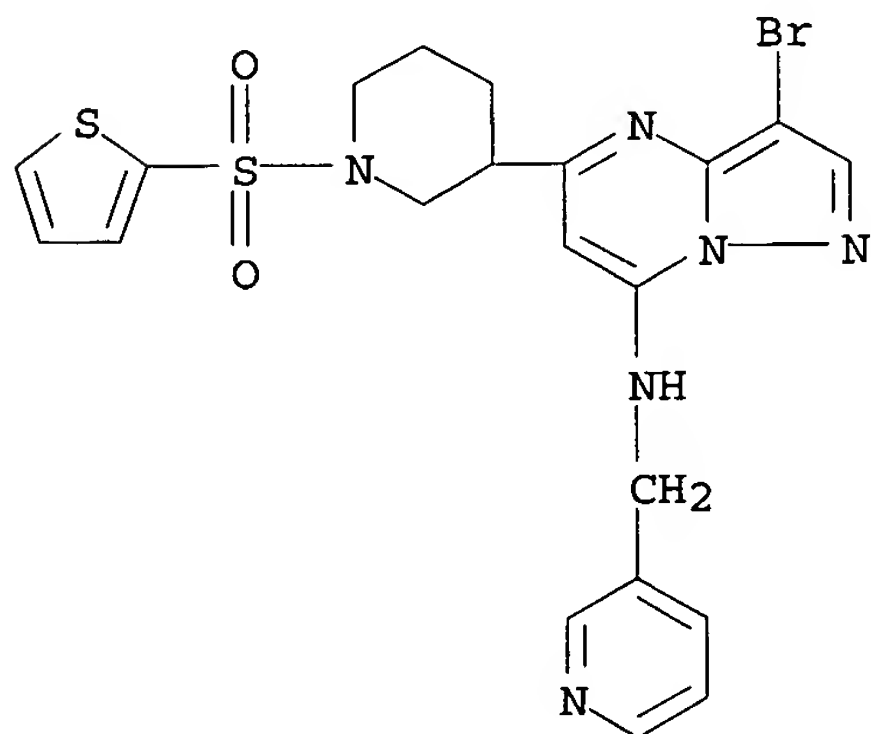
CN Piperidine, 1-[[3,5-bis(trifluoromethyl)phenyl]sulfonyl]-4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-(9CI) (CA INDEX NAME)



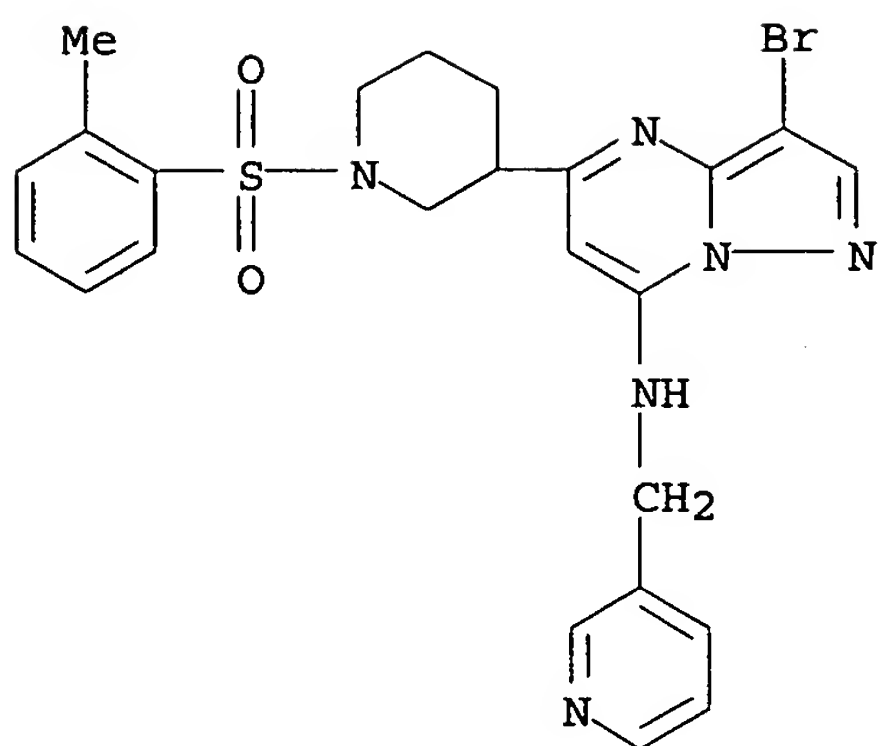
RN 677794-02-4 HCAPLUS  
 CN Piperidine, 4-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



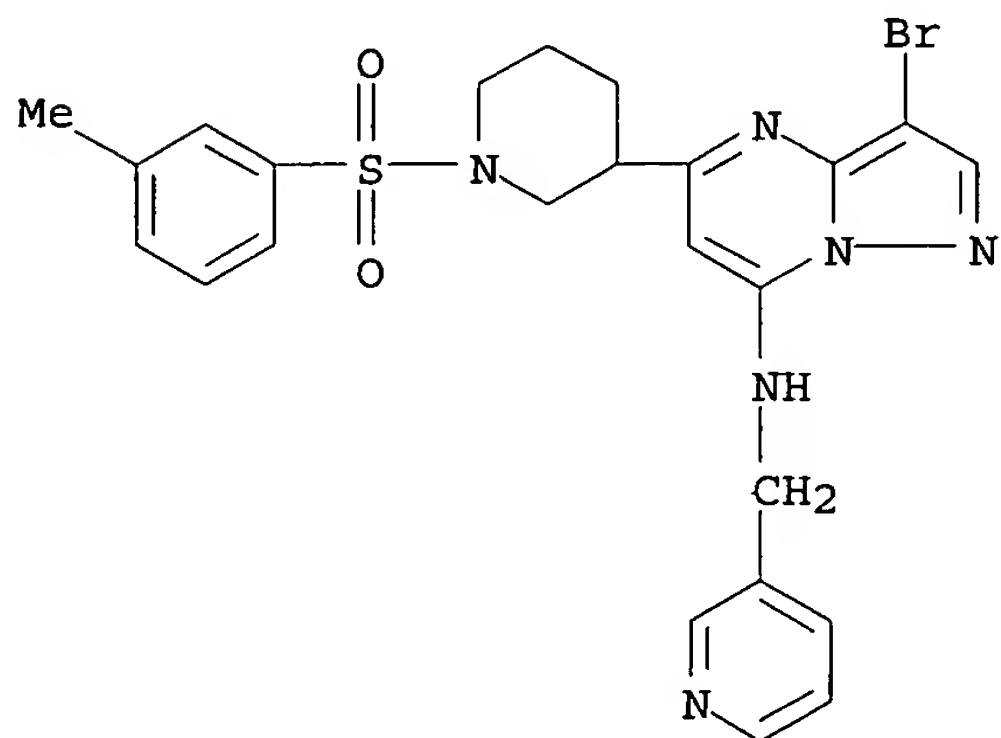
RN 677794-03-5 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)



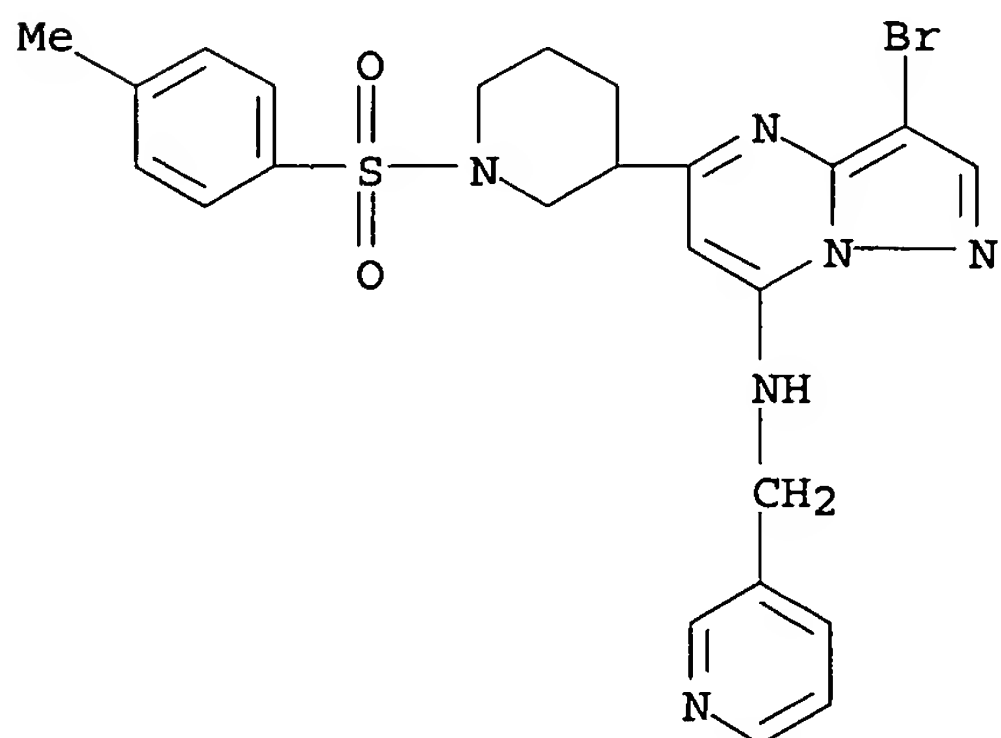
RN 677794-04-6 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-05-7 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

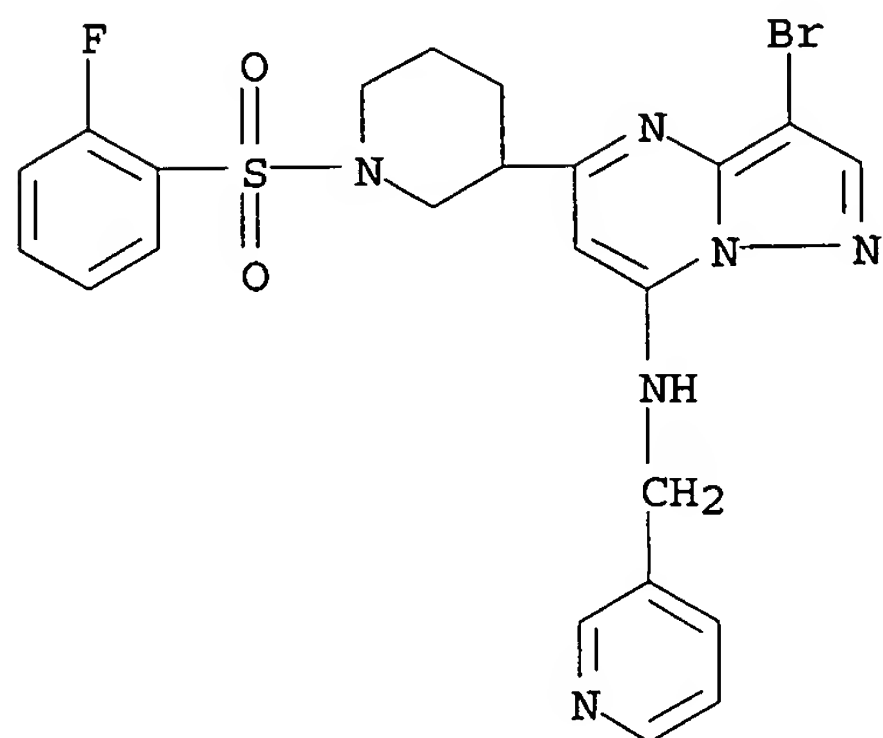


RN 677794-06-8 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



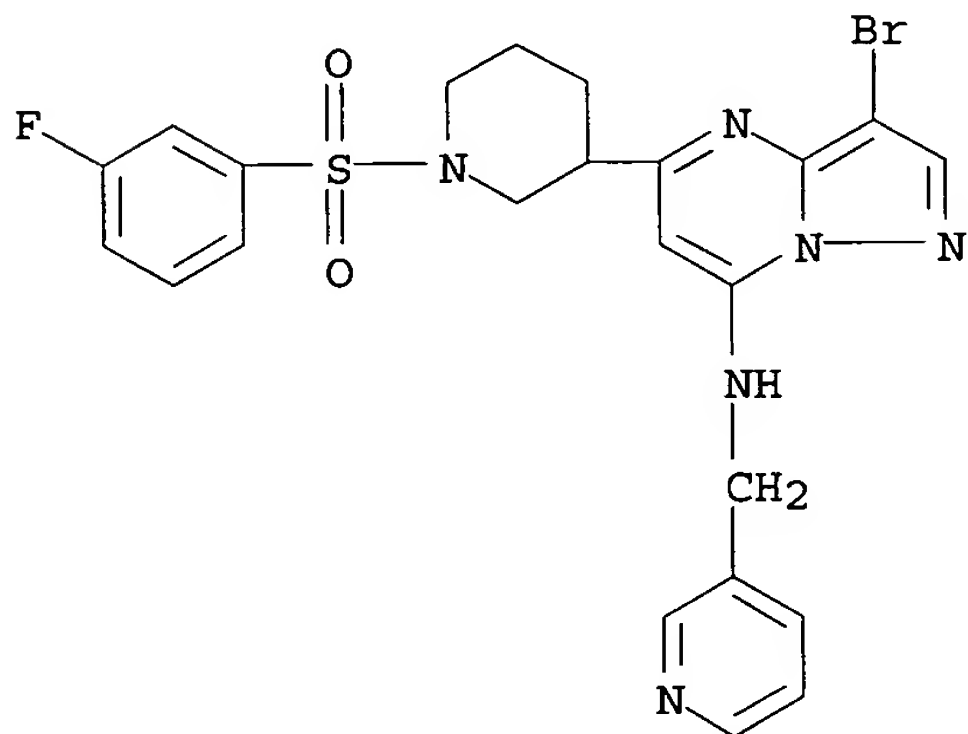
RN 677794-07-9 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-08-0 HCAPLUS

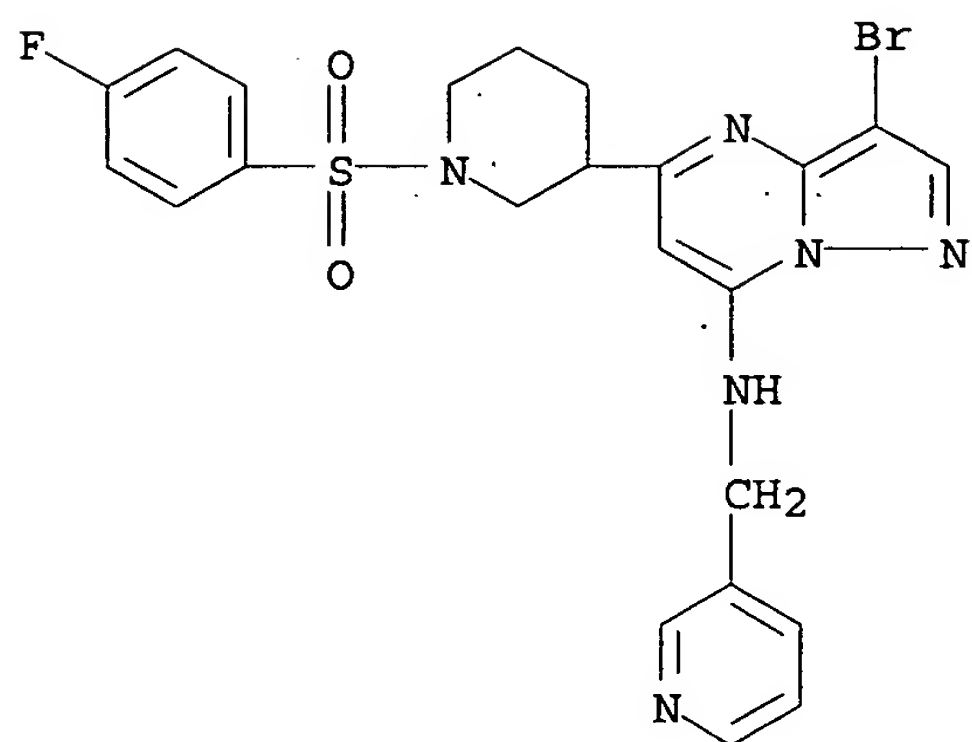
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-09-1 HCAPLUS

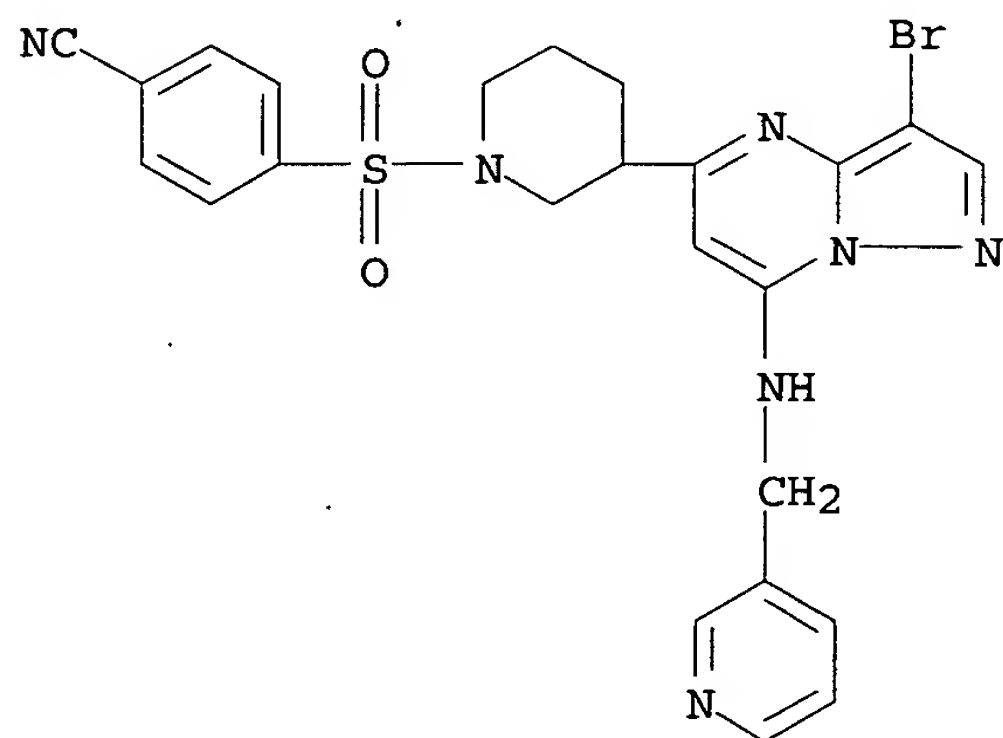
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)





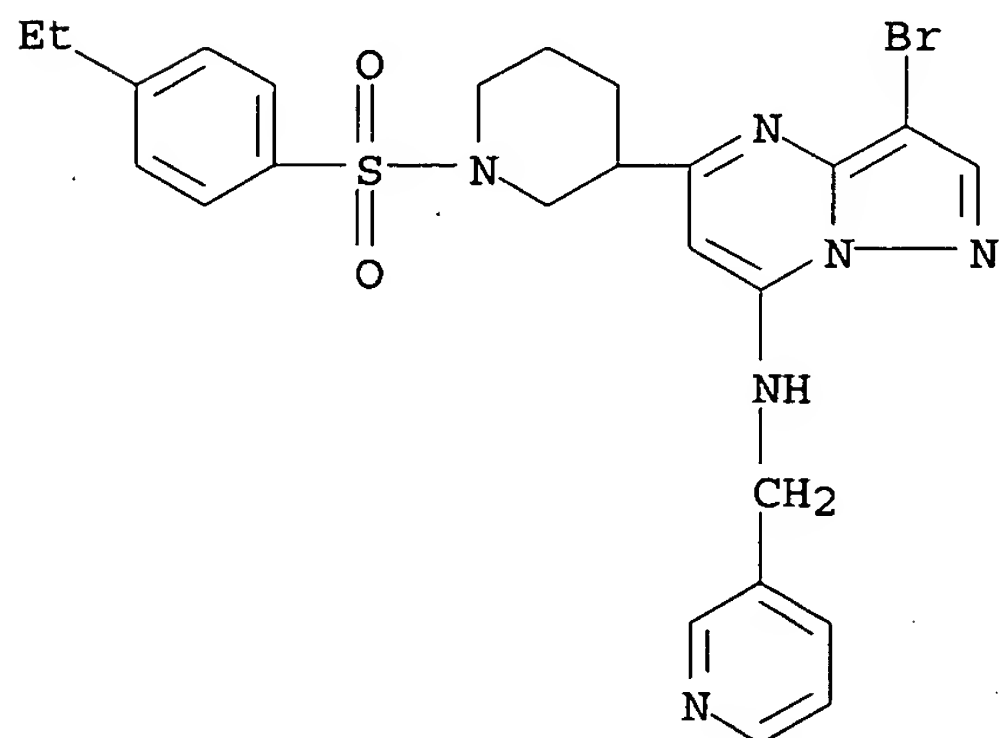
RN 677794-10-4 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-cyanophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



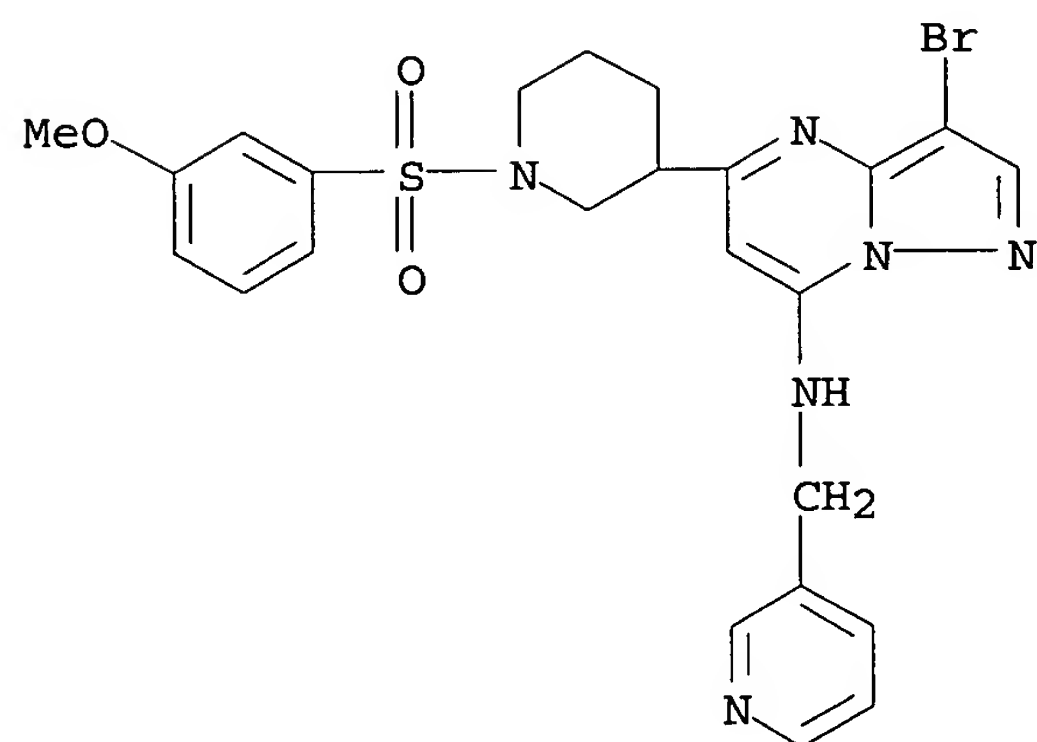
RN 677794-12-6 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-ethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



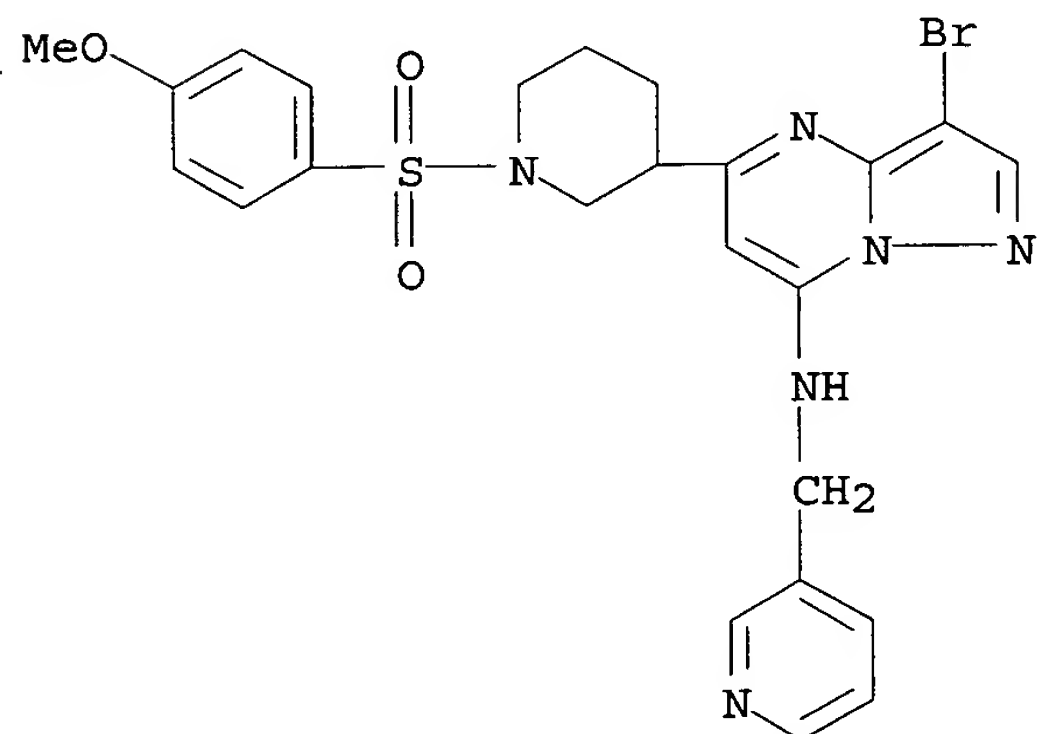
RN 677794-13-7 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



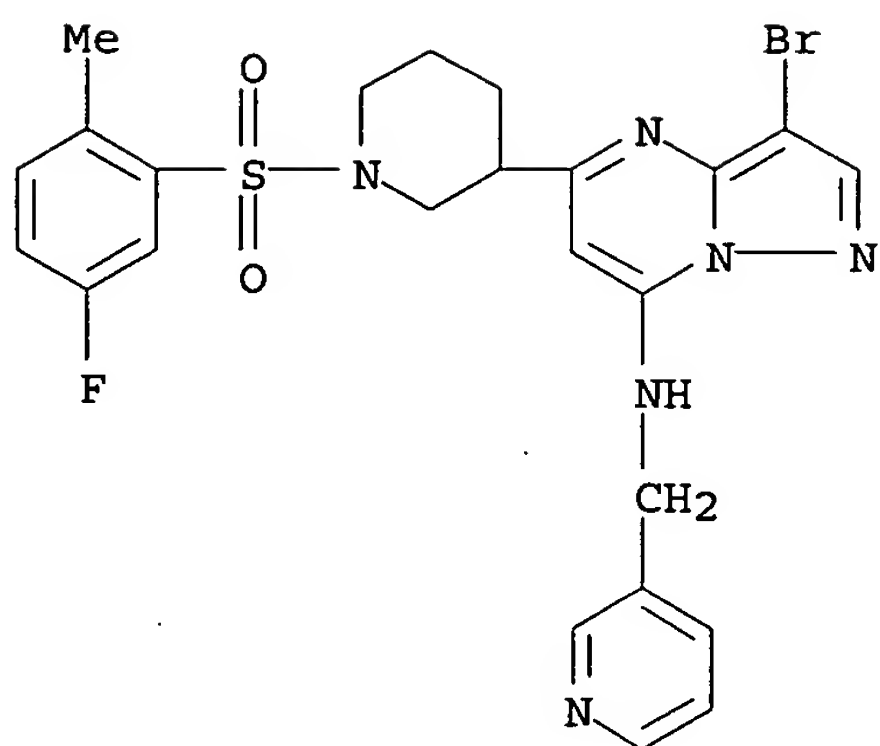
RN 677794-14-8 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



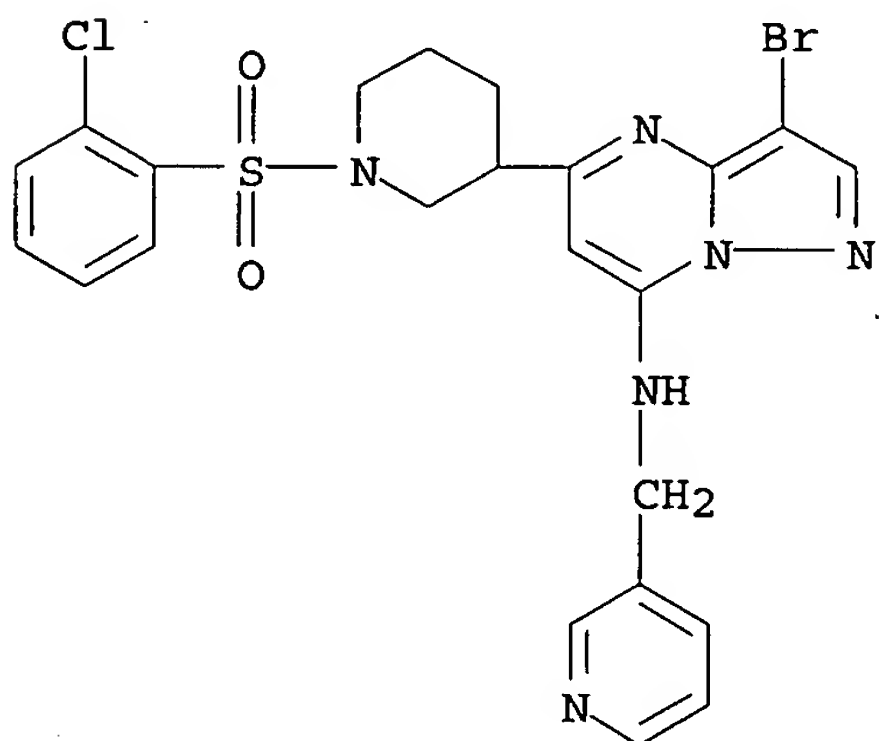
RN 677794-15-9 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-fluoro-2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



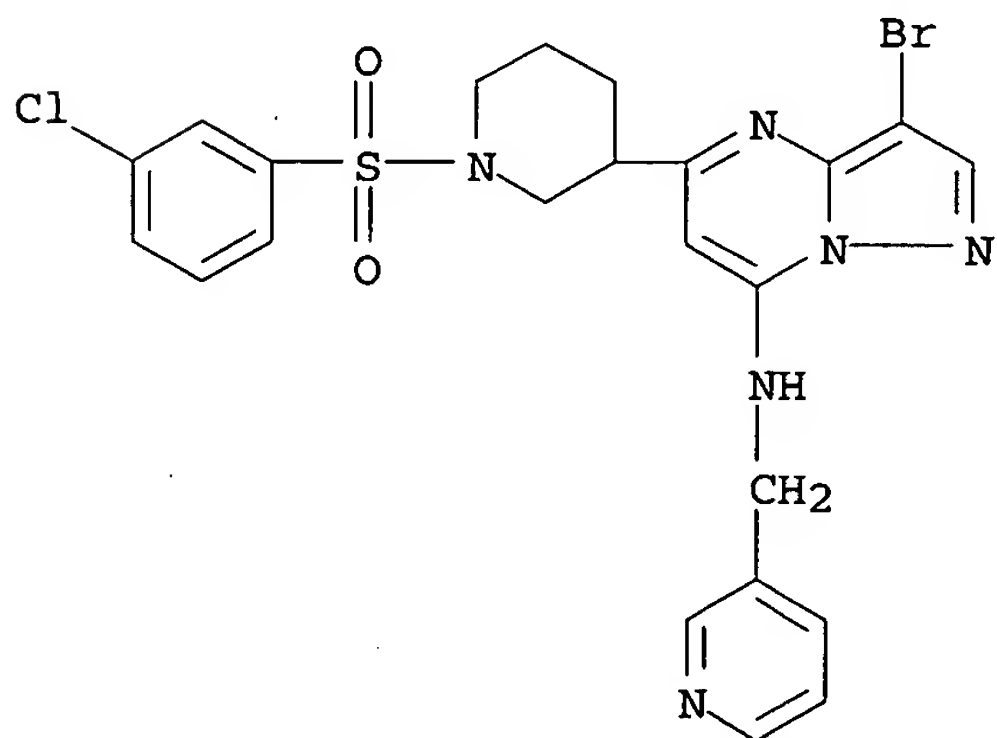
RN 677794-16-0 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



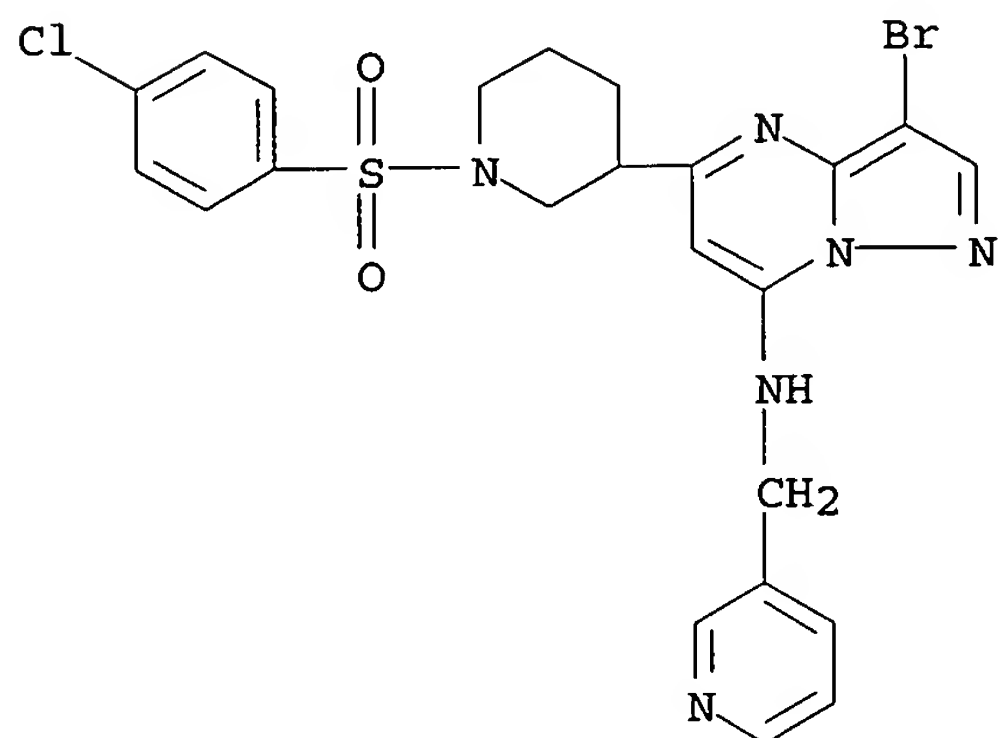
RN 677794-17-1 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

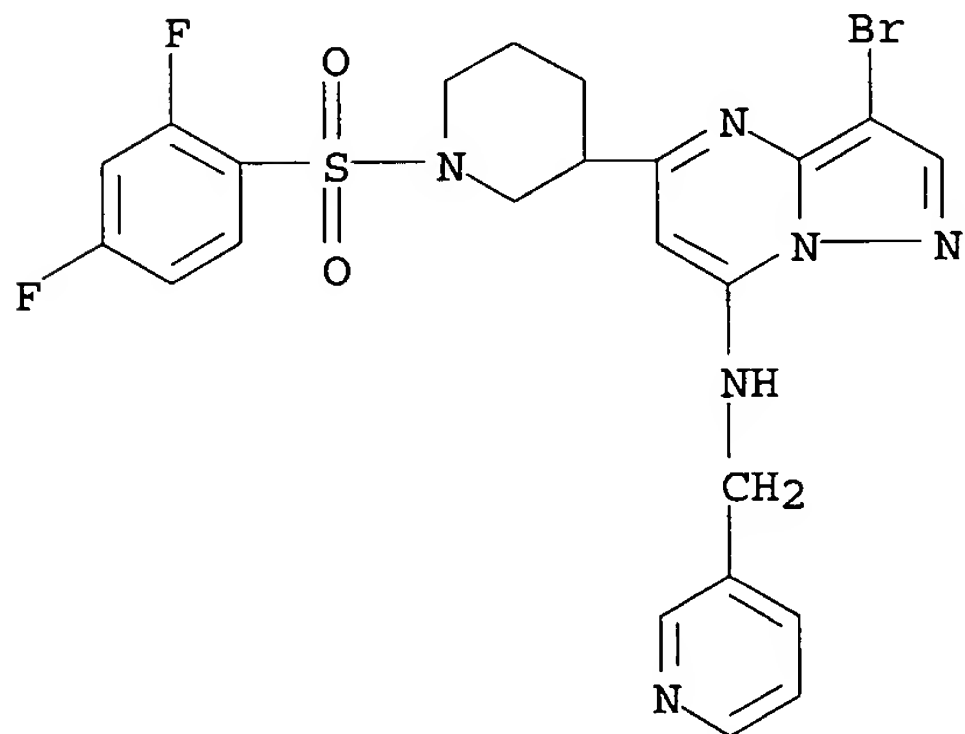


RN 677794-18-2 HCAPLUS

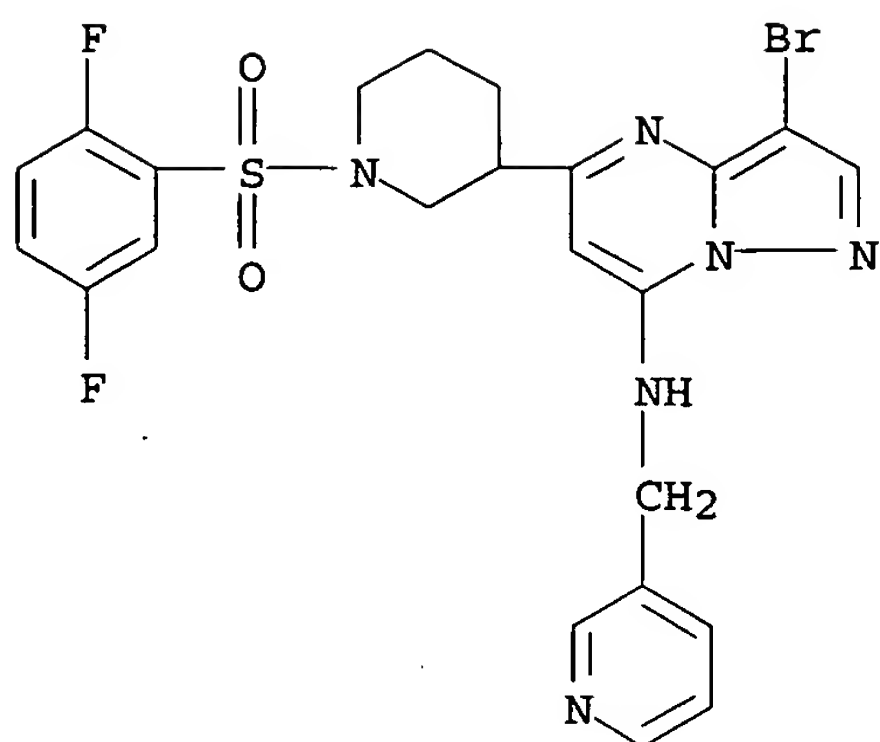
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



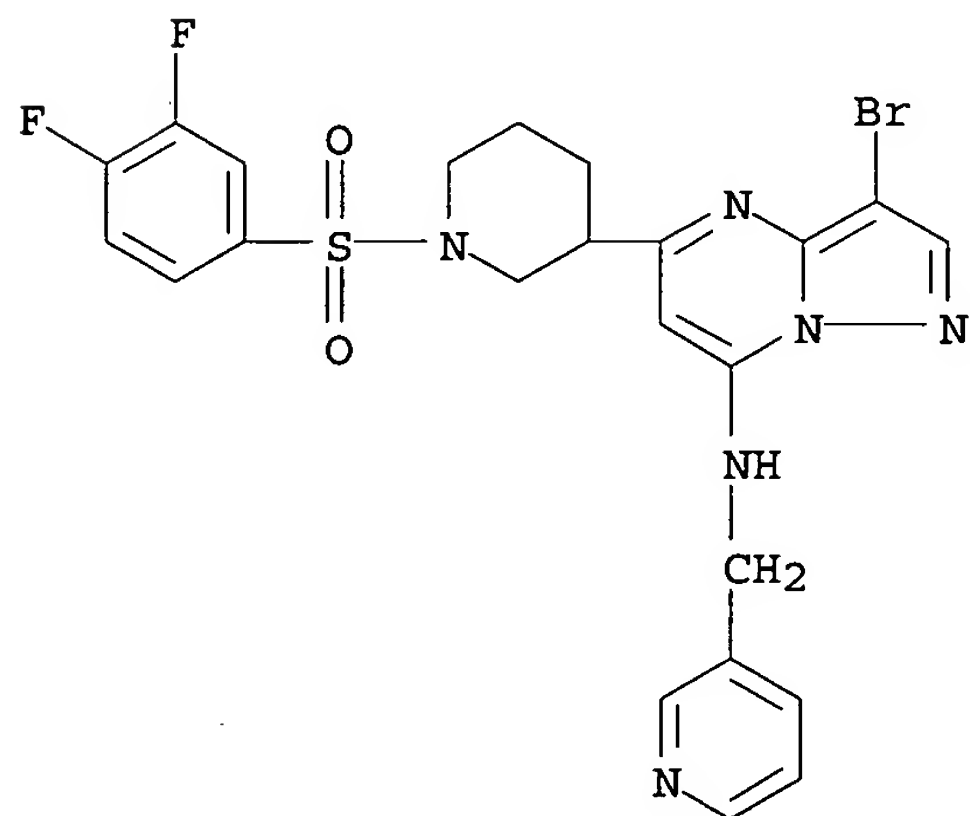
RN 677794-19-3 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



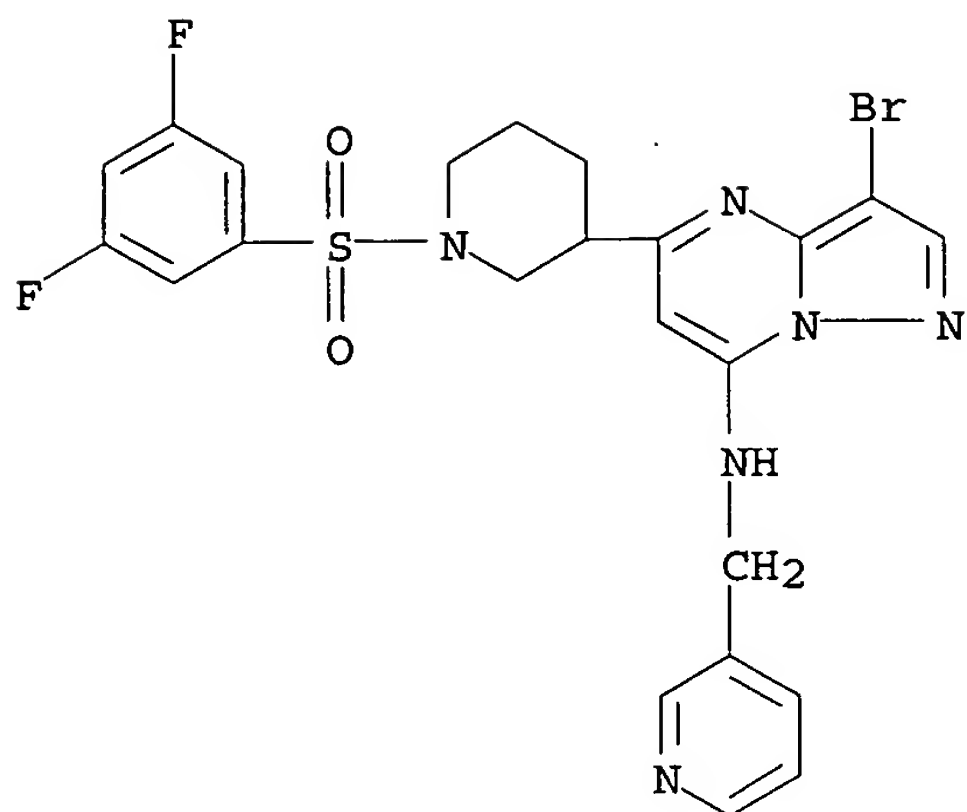
RN 677794-20-6 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



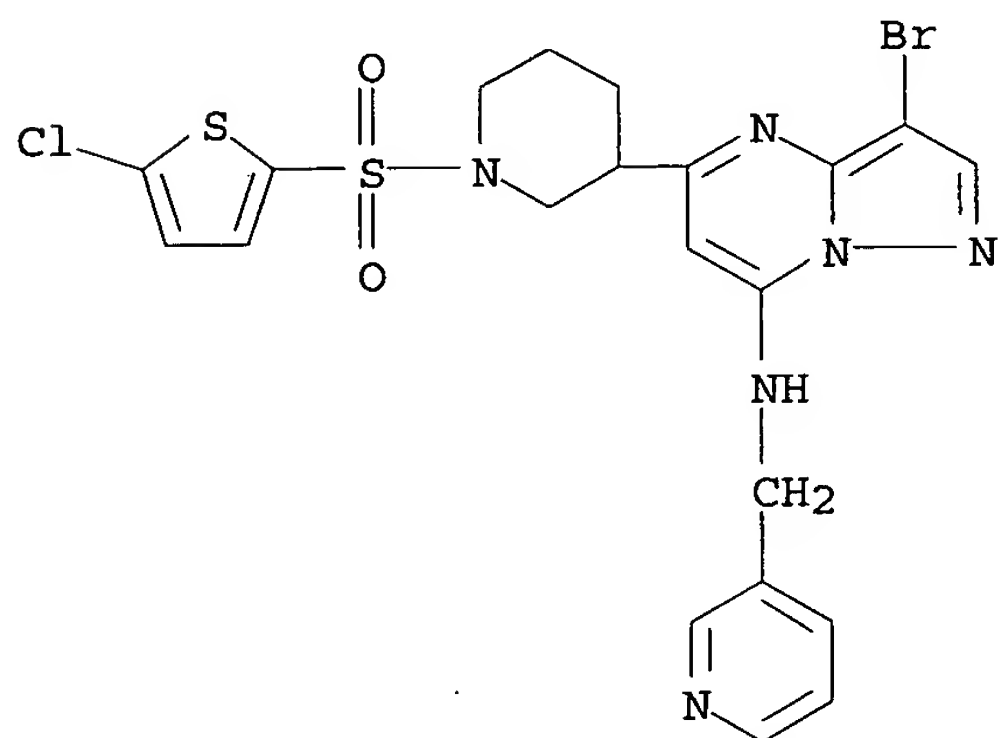
RN 677794-21-7 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



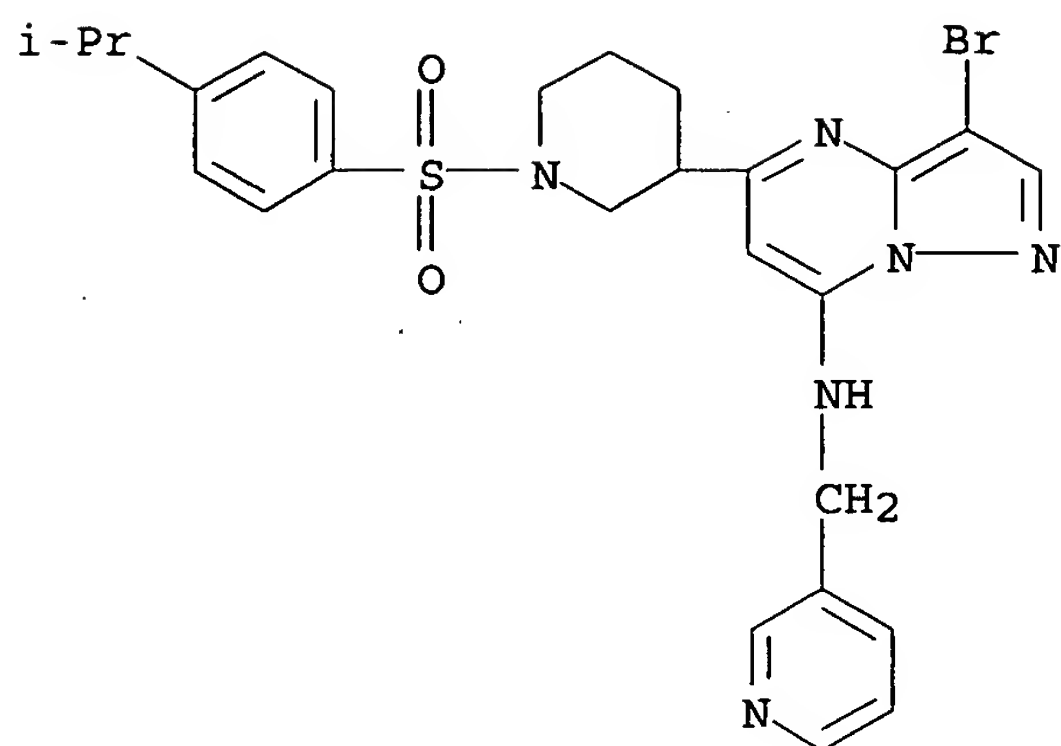
RN 677794-22-8 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,5-difluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 677794-23-9 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)aminolpyrazolo[1,5-a]pyrimidin-5-yl]-1-[(5-chloro-2-thienyl)sulfonyl]- (9CI) (CA INDEX NAME)

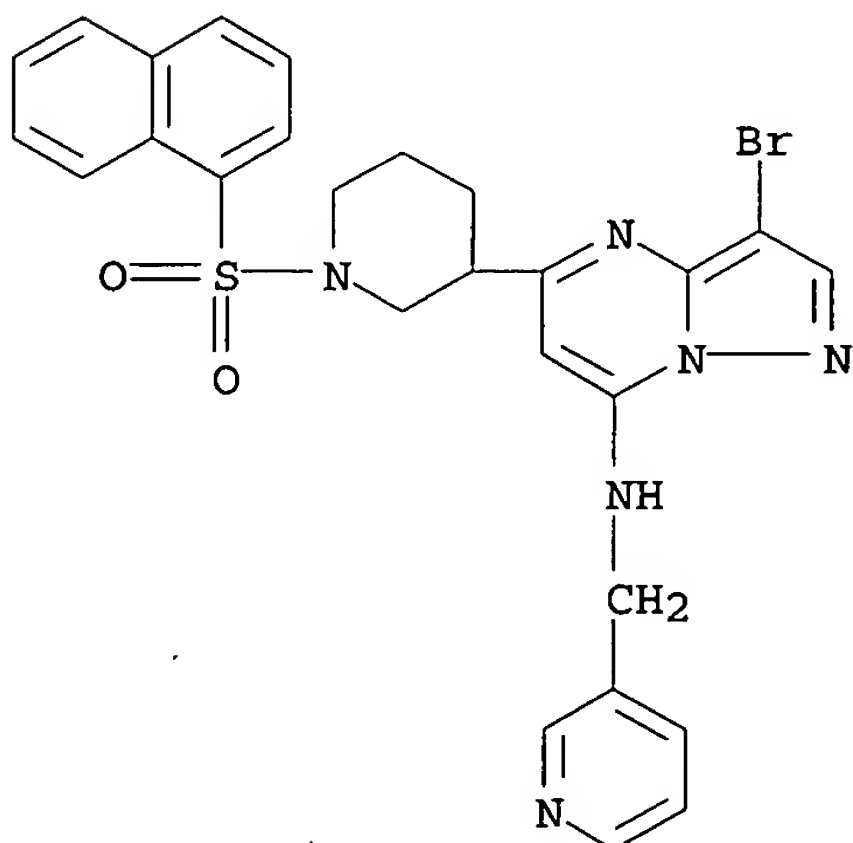


RN 677794-24-0 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)aminolpyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1-methylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



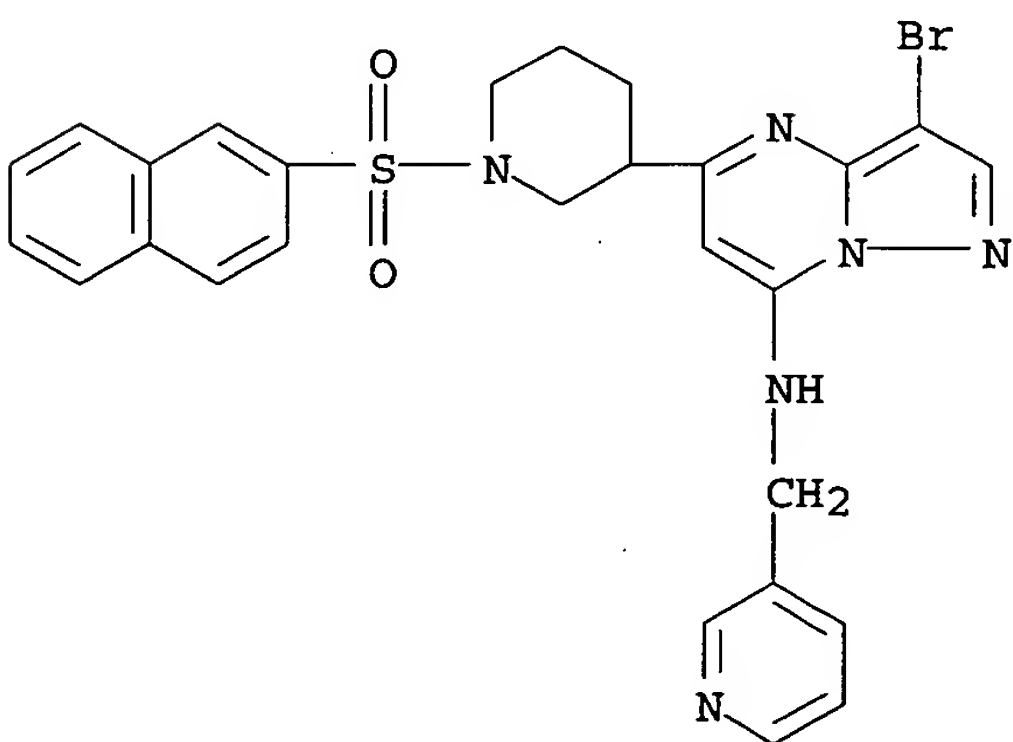
RN 677794-25-1 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

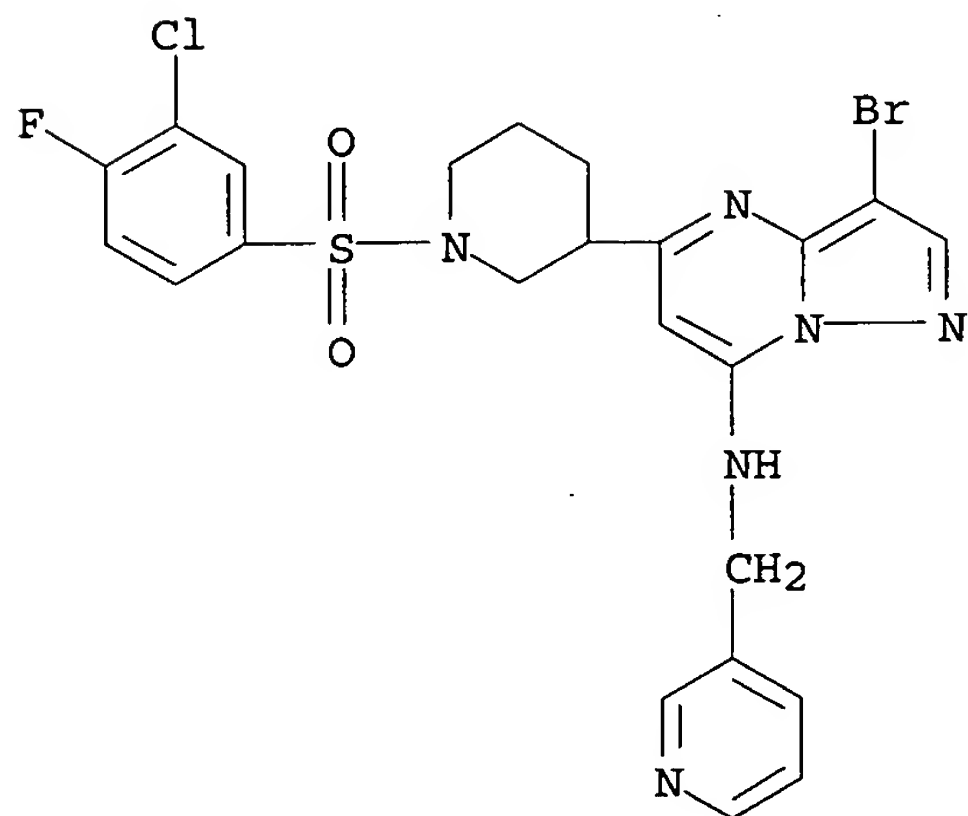


RN 677794-26-2 HCAPLUS

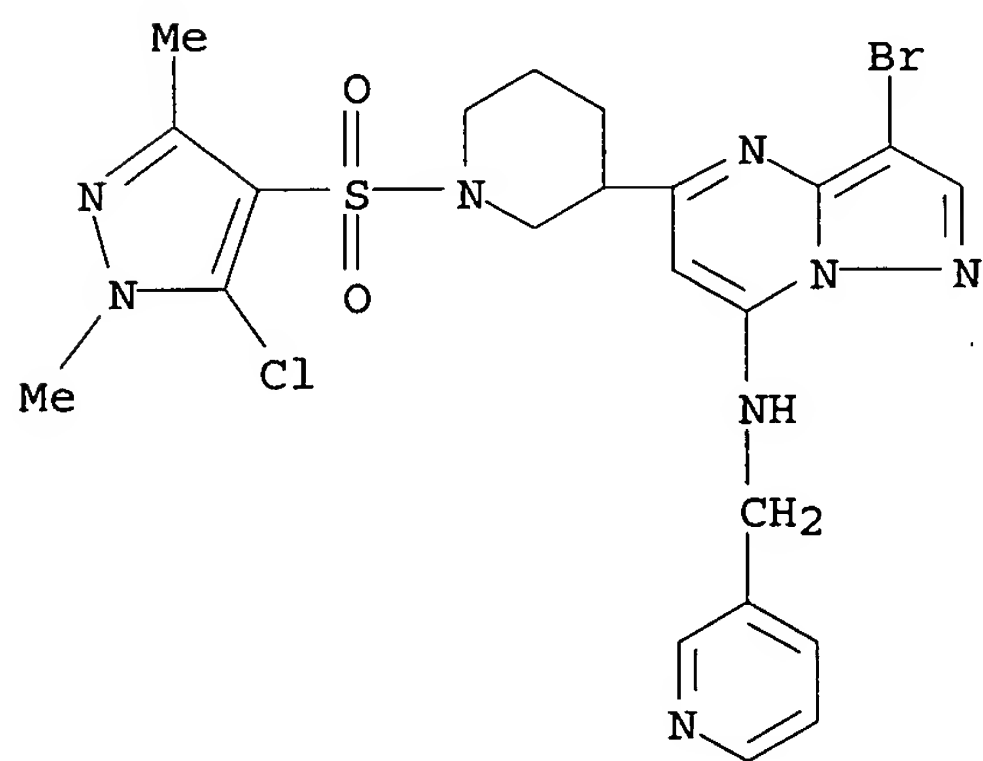
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-(2-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)



RN 677794-27-3 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-  
 a]pyrimidin-5-yl]-1-[(3-chloro-4-fluorophenyl)sulfonyl]- (9CI) (CA INDEX  
 NAME)

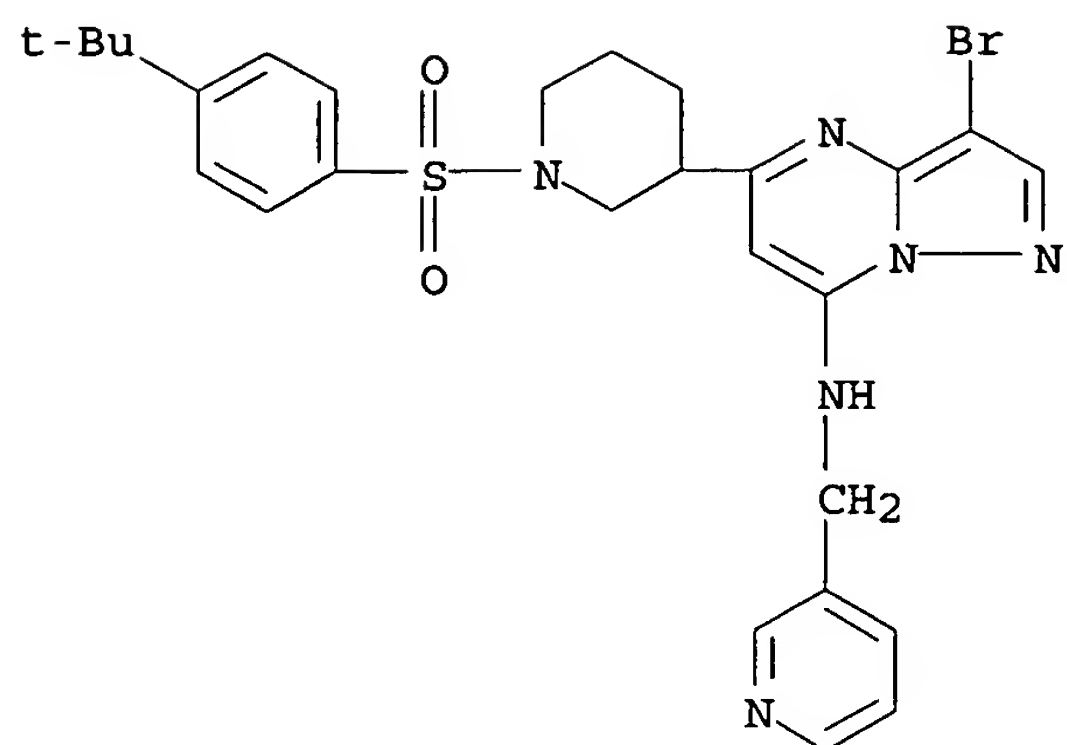


RN 677794-28-4 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-  
 a]pyrimidin-5-yl]-1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-  
 (9CI) (CA INDEX NAME)



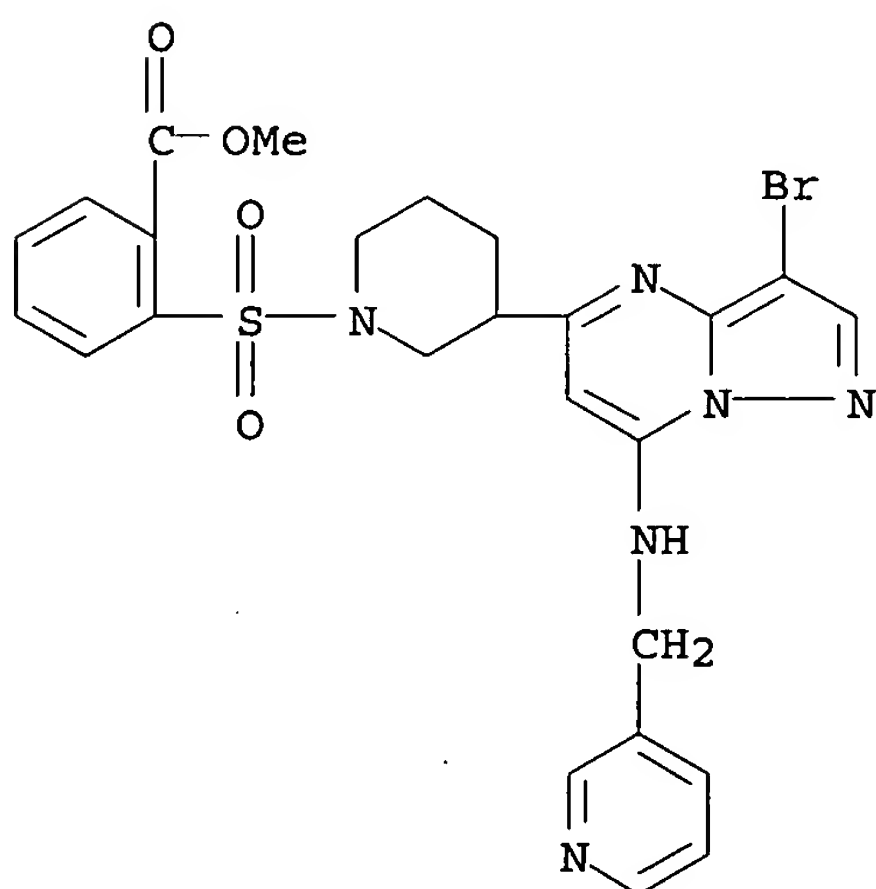
RN 677794-29-5 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-  
 a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylethyl)phenyl]sulfonyl]- (9CI) (CA  
 INDEX NAME)





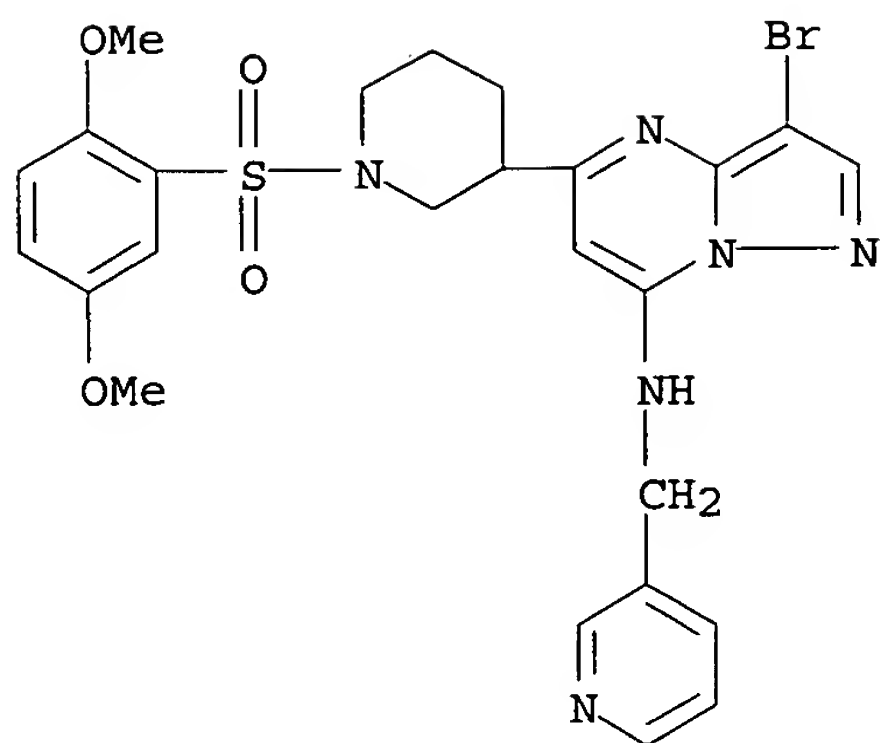
RN 677794-30-8 HCAPLUS

CN Benzoic acid, 2-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

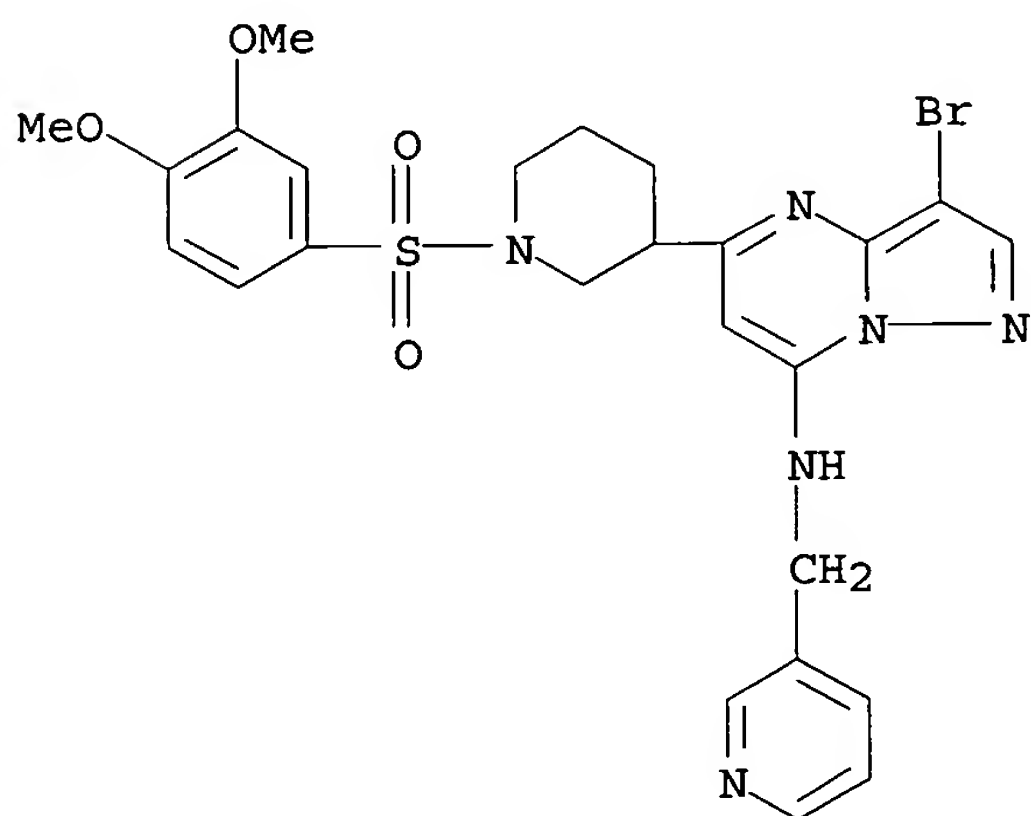


RN 677794-31-9 HCAPLUS

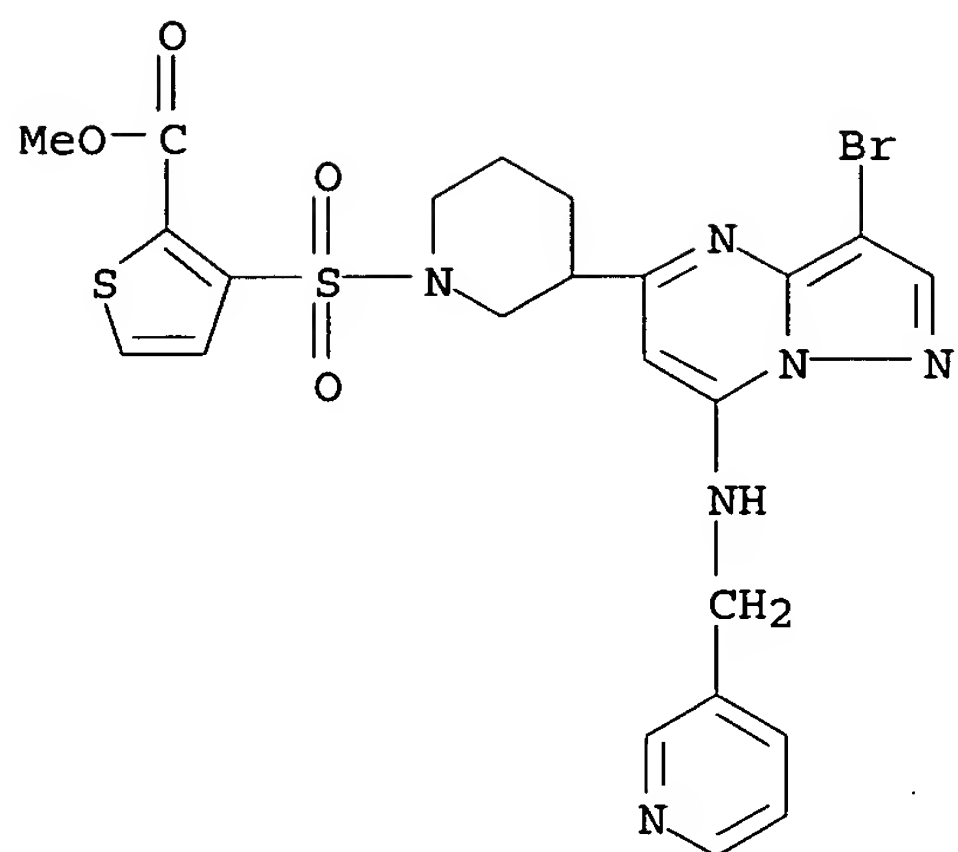
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



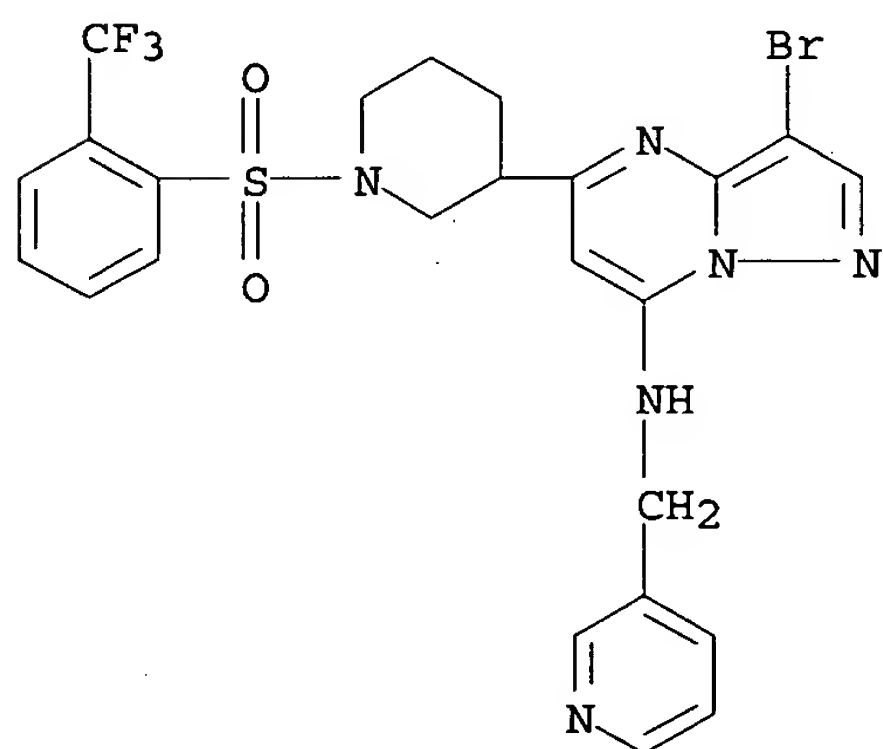
RN 677794-32-0 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



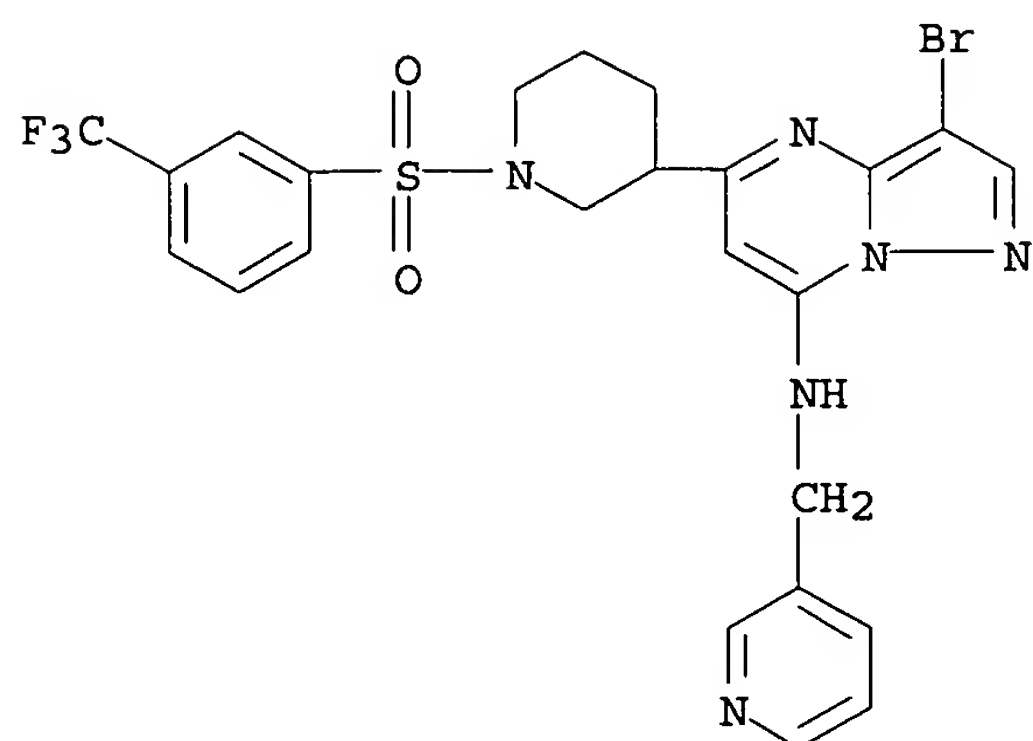
RN 677794-33-1 HCAPLUS  
 CN 2-Thiophenecarboxylic acid, 3-[[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 677794-34-2 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[2-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

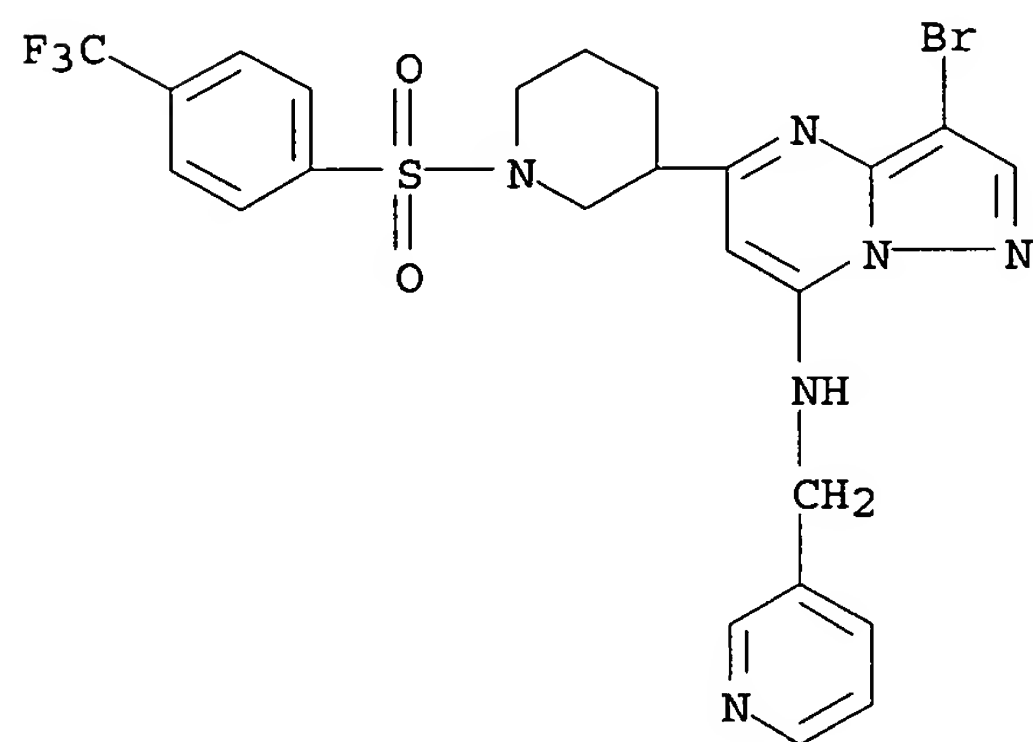


RN 677794-35-3 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



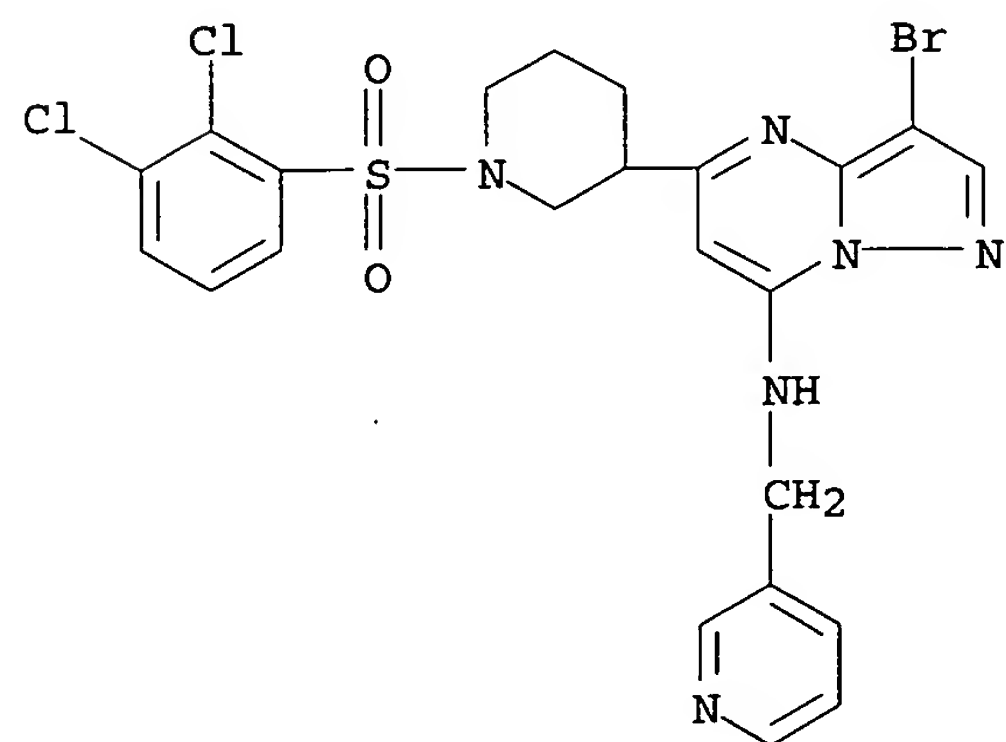
RN 677794-36-4 HCAPLUS

CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

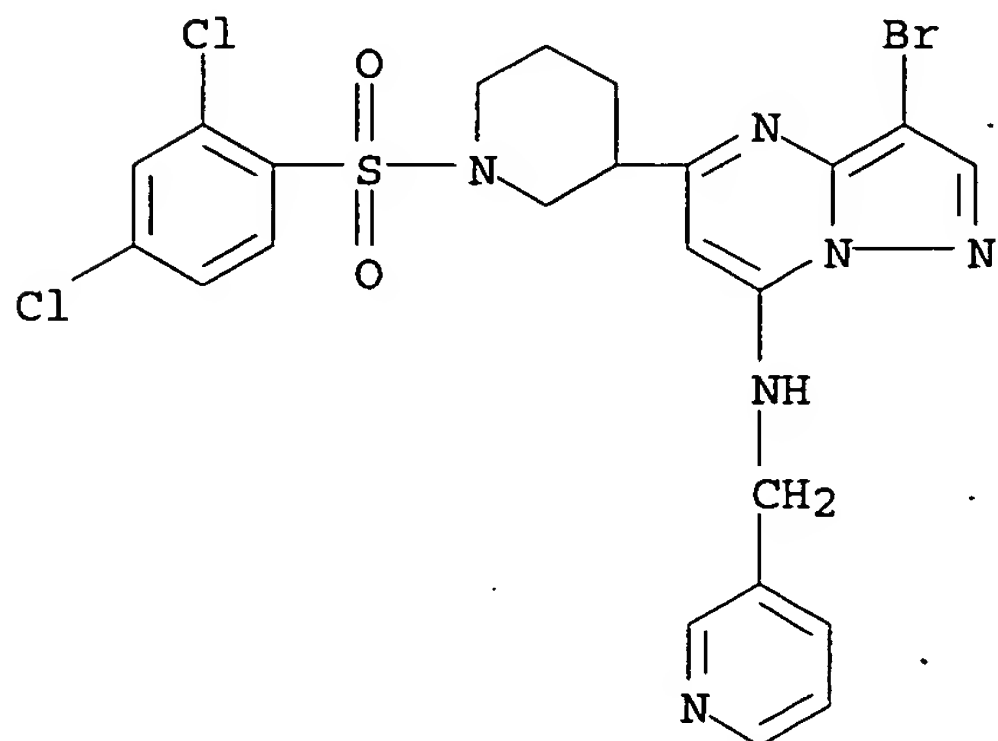


RN 677794-37-5 HCAPLUS

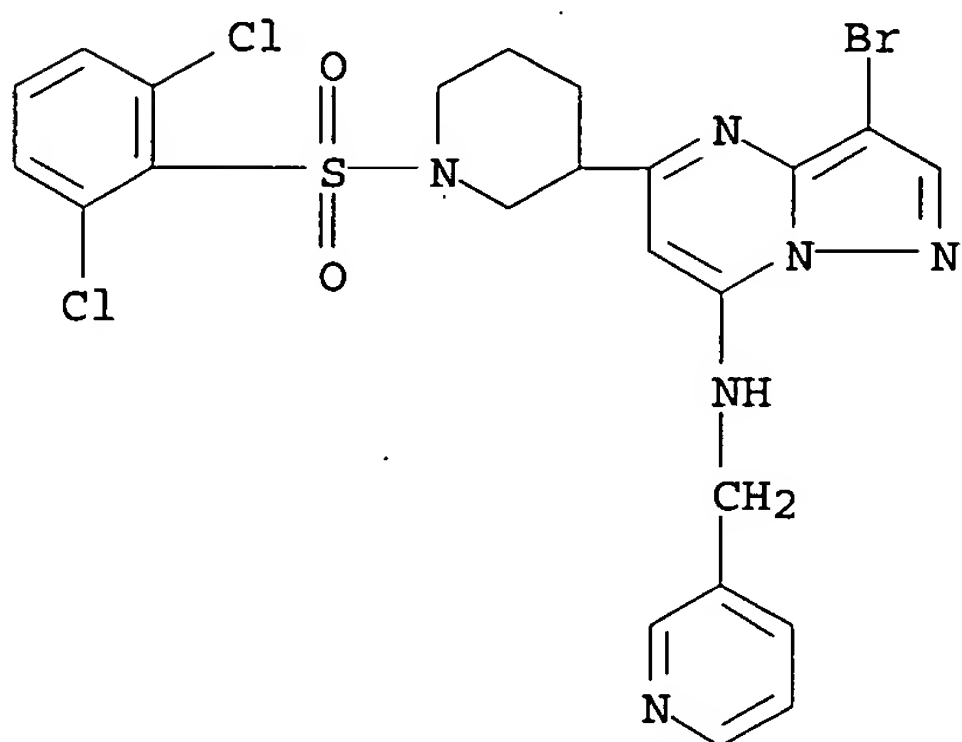
CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,3-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



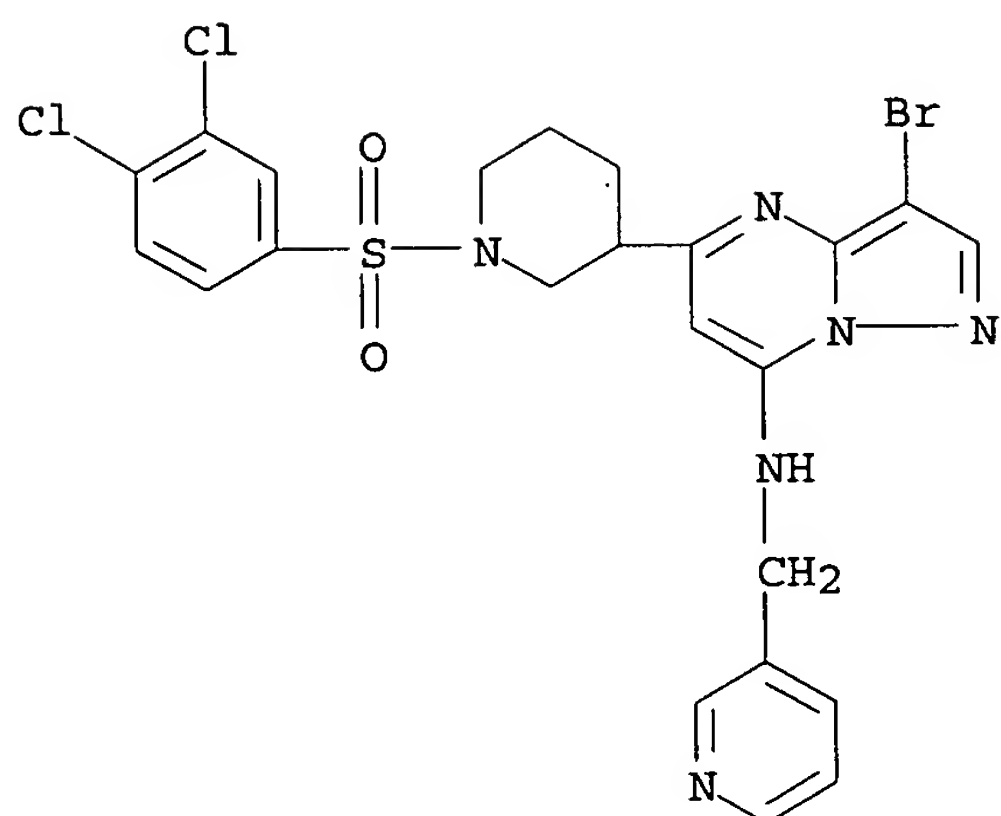
RN 677794-38-6 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



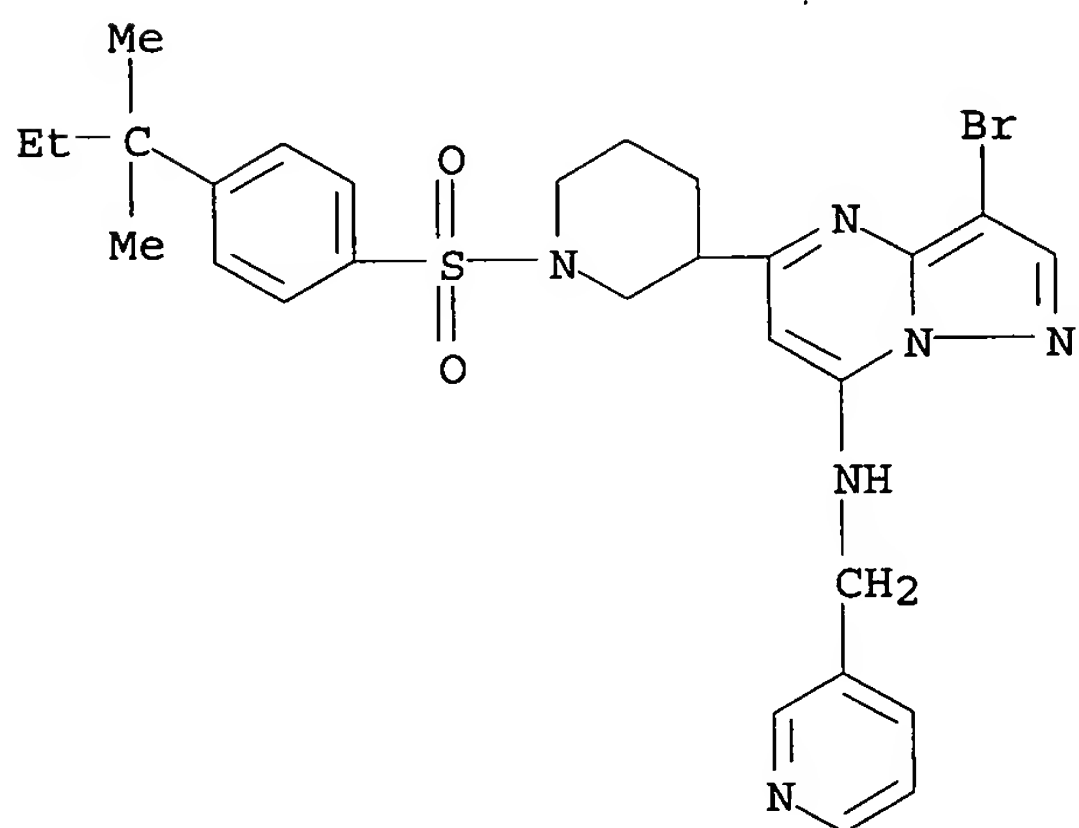
RN 677794-39-7 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,6-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



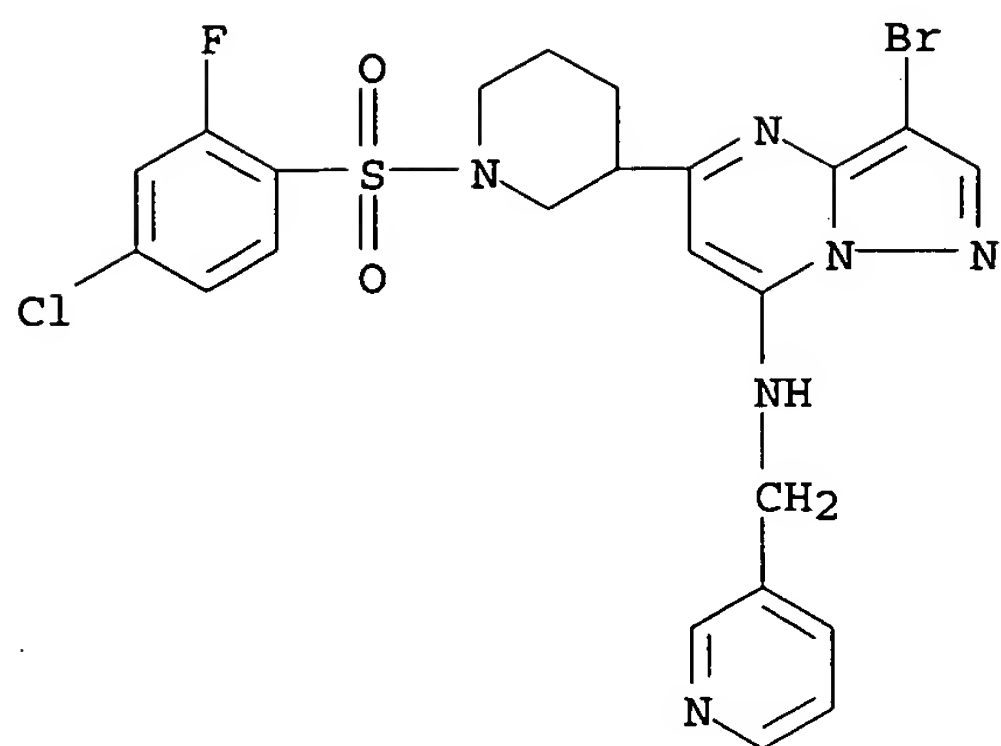
RN 677794-40-0 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(3,4-dichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



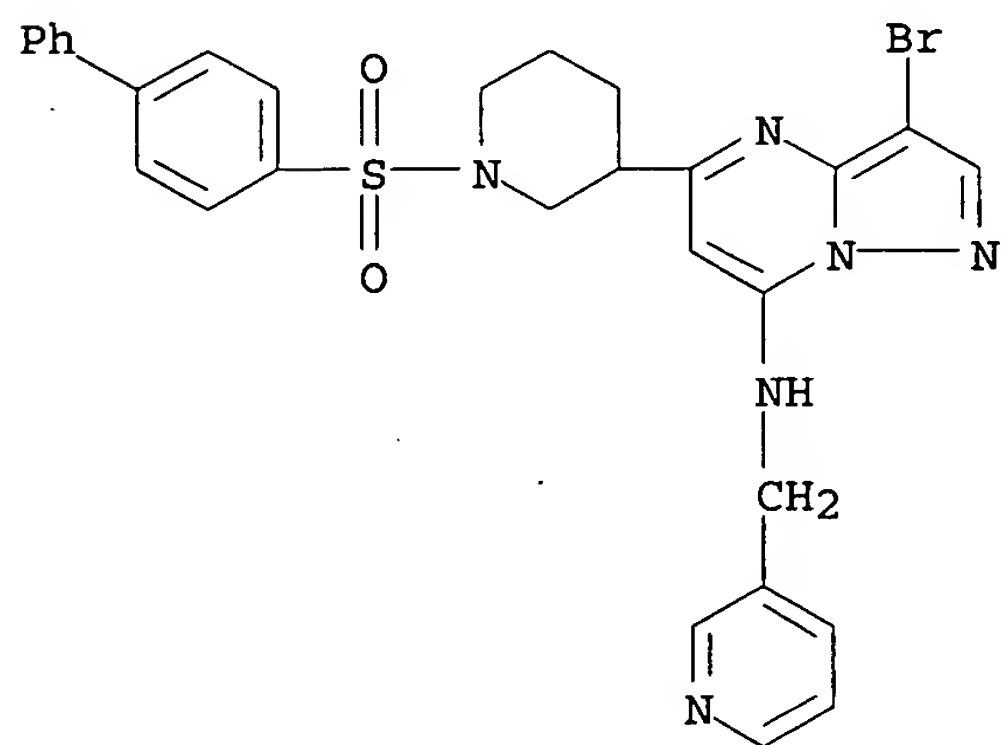
RN 677794-41-1 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(1,1-dimethylpropyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



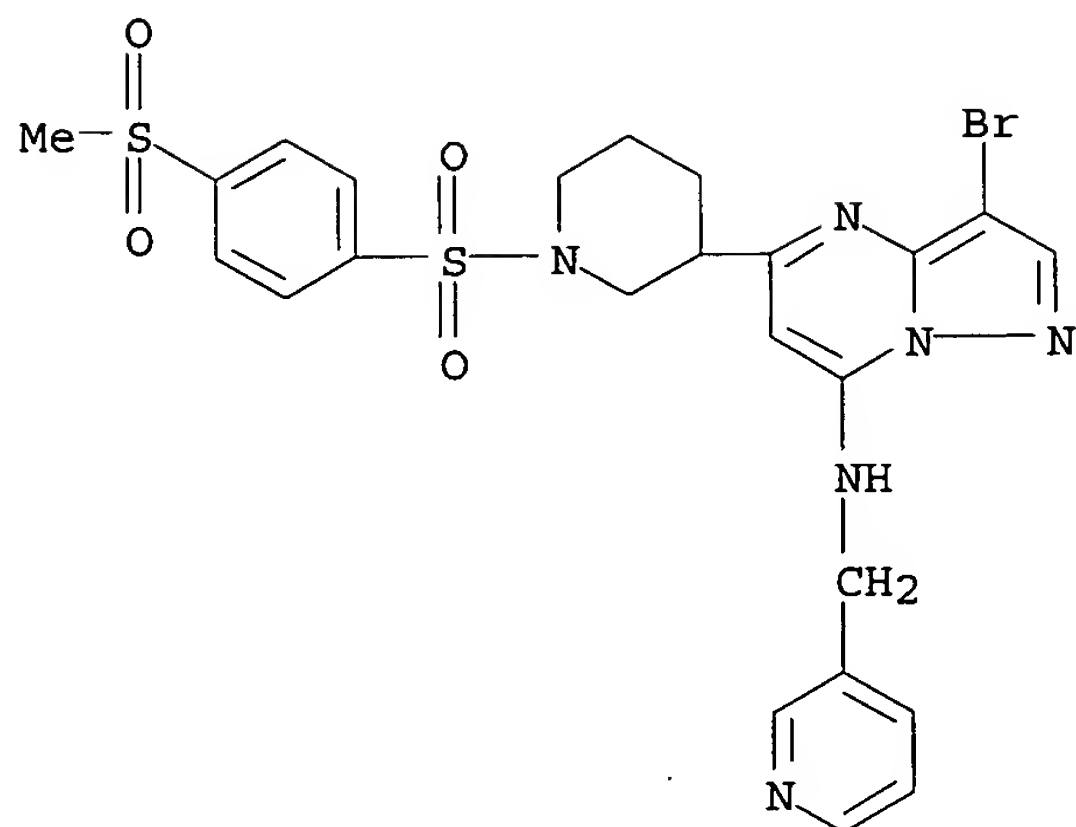
RN 677794-42-2 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-chloro-2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



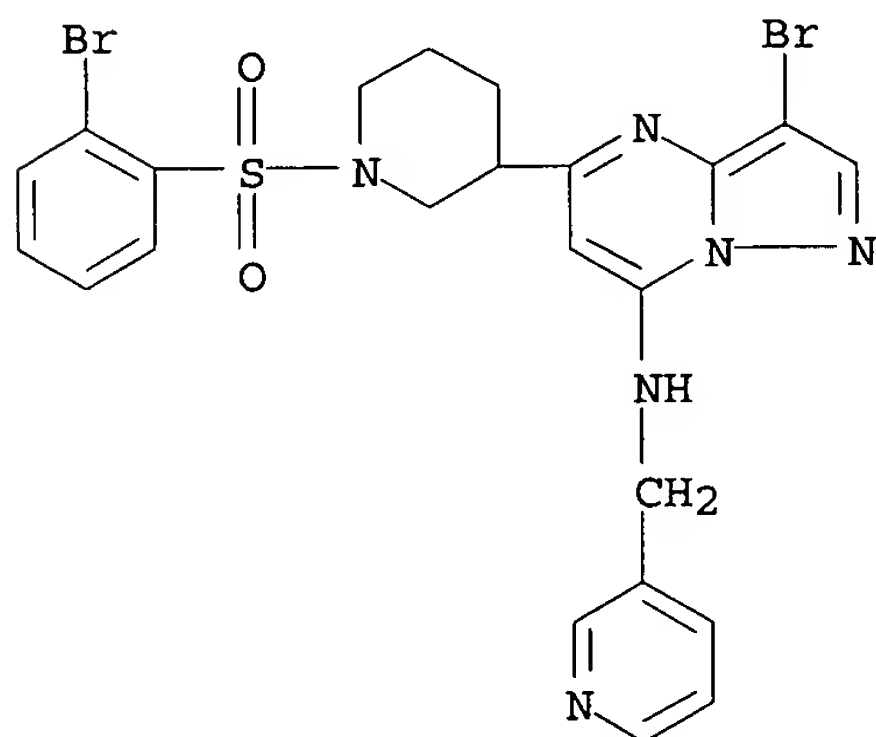
RN 677794-43-3 HCAPLUS  
 CN Piperidine, 1-([1,1'-biphenyl]-4-ylsulfonyl)-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)



RN 677794-44-4 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(methylsulfonyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

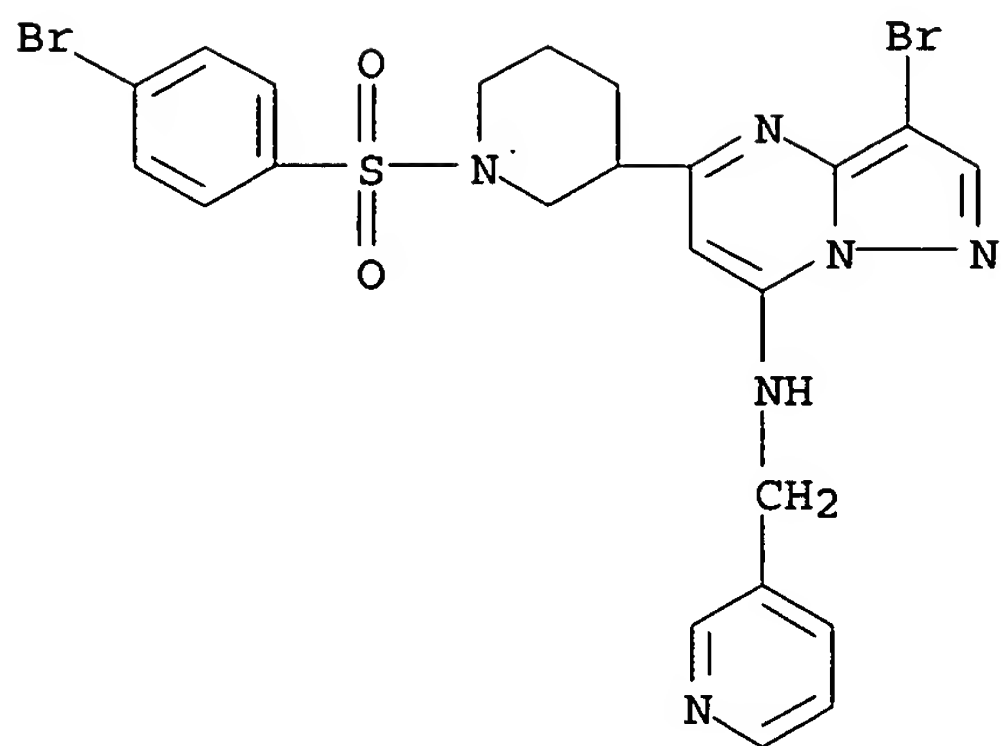


RN 677794-45-5 HCAPLUS  
 CN Piperidine, 1-[(2-bromophenyl)sulfonyl]-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

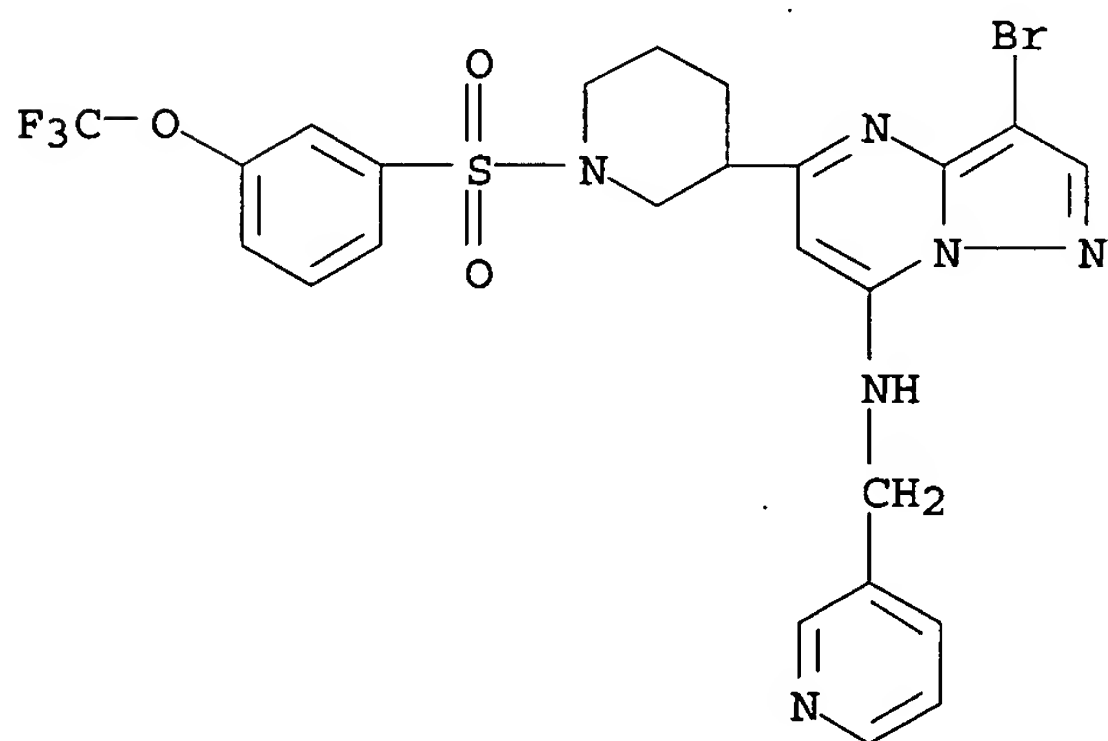


RN 677794-46-6 HCAPLUS  
 CN Piperidine, 1-[(4-bromophenyl)sulfonyl]-3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]- (9CI) (CA INDEX NAME)

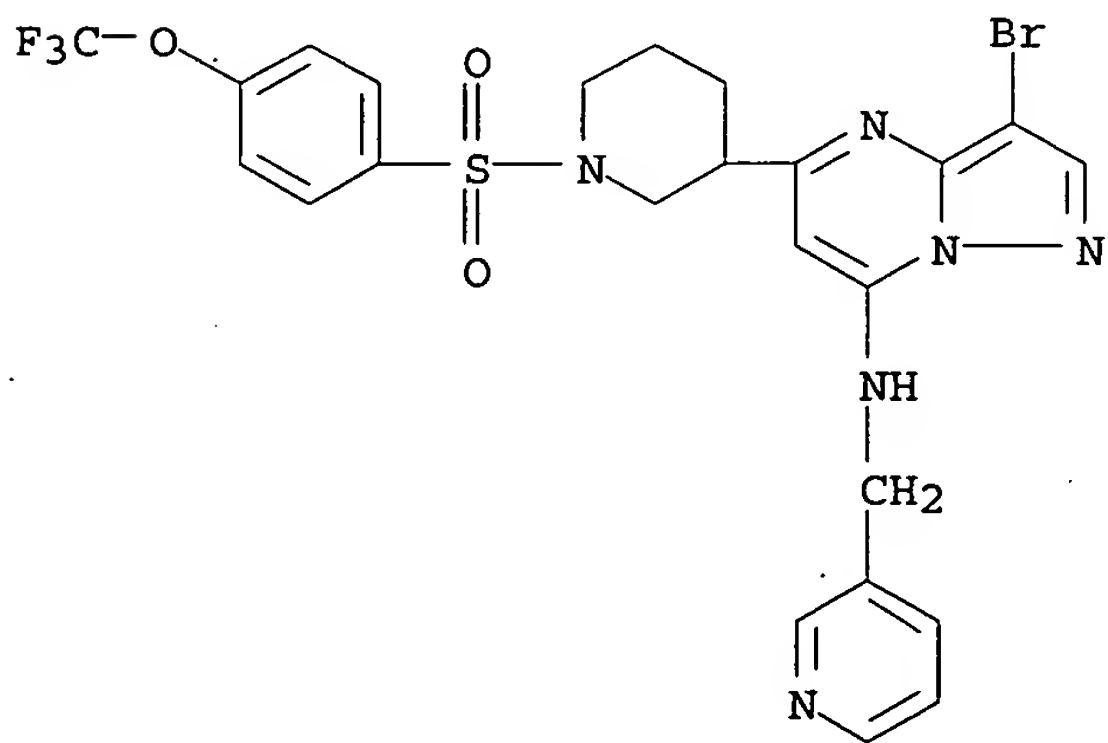




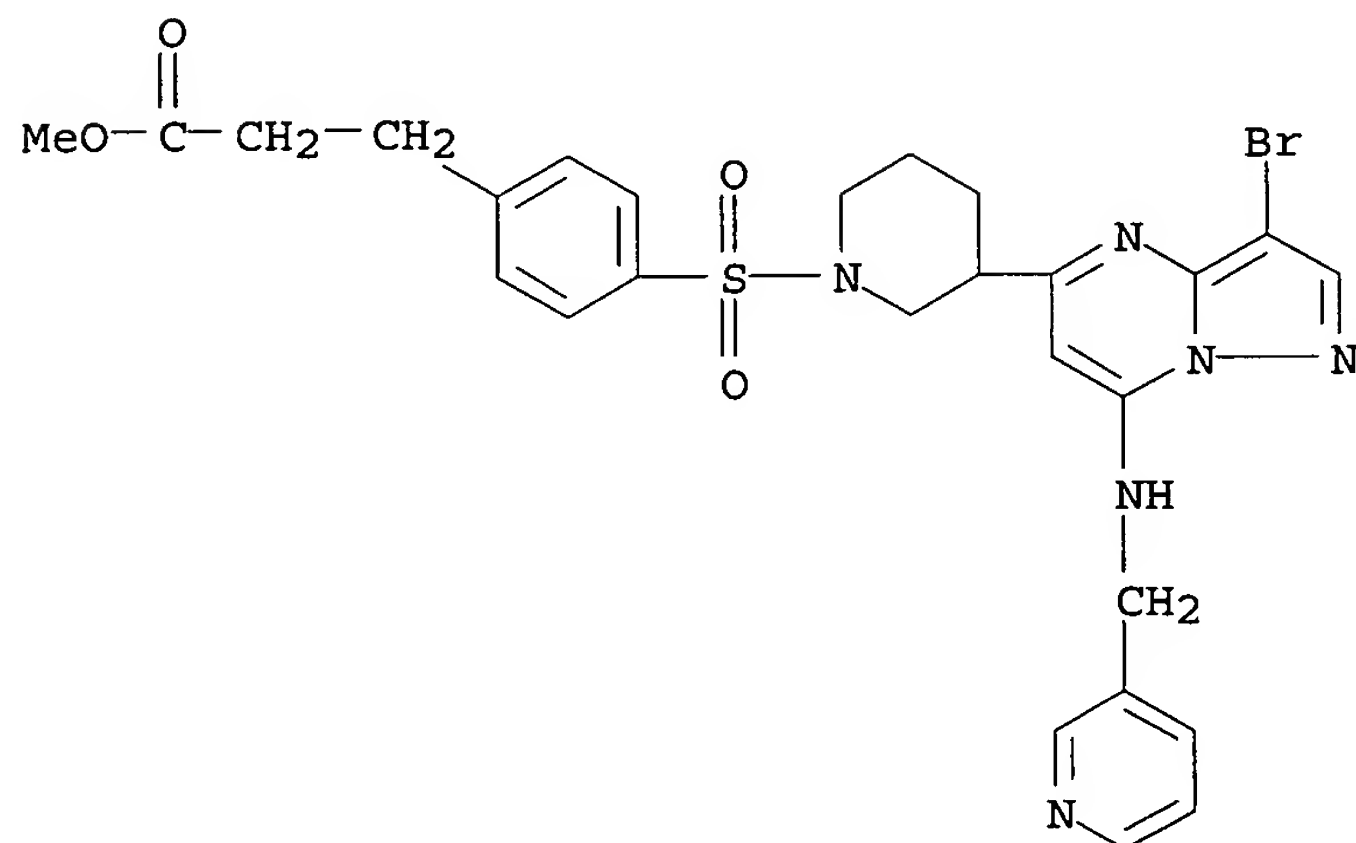
RN 677794-47-7 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[3-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



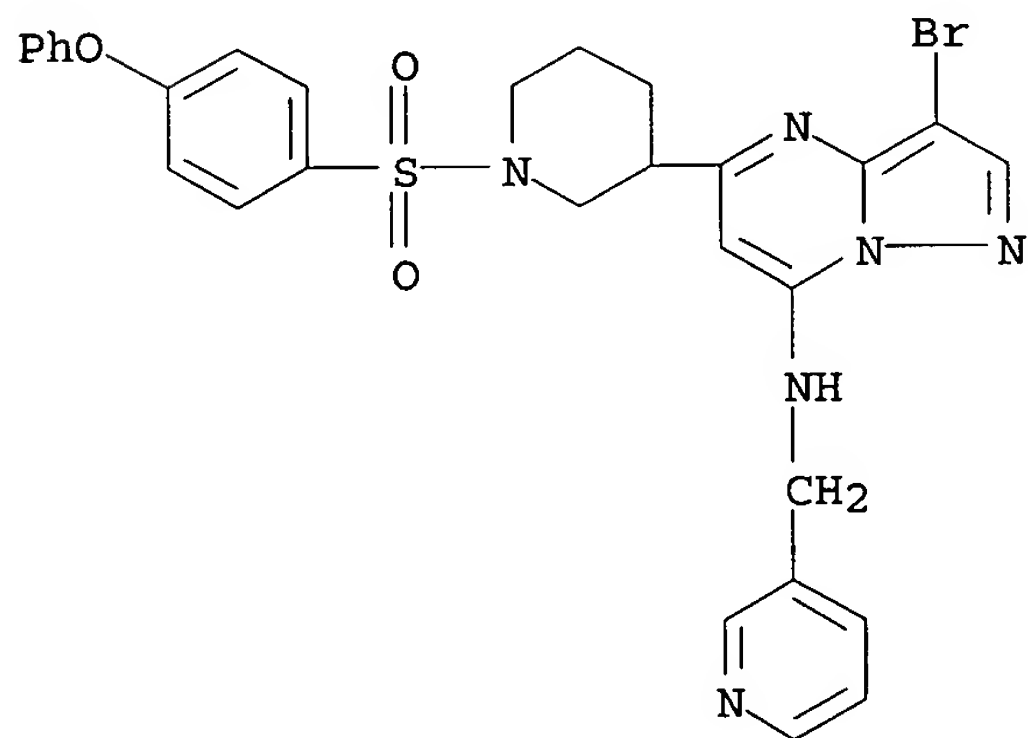
RN 677794-48-8 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



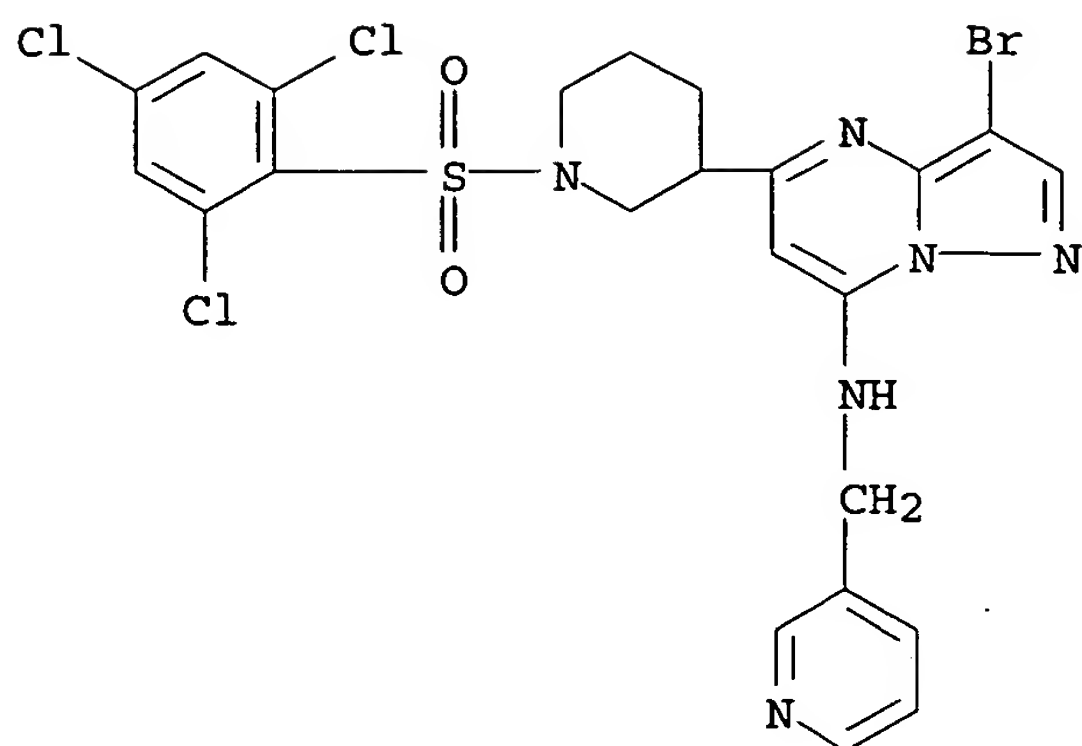
RN 677794-49-9 HCAPLUS  
 CN Benzenepropanoic acid, 4-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 677794-50-2 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(4-phenoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

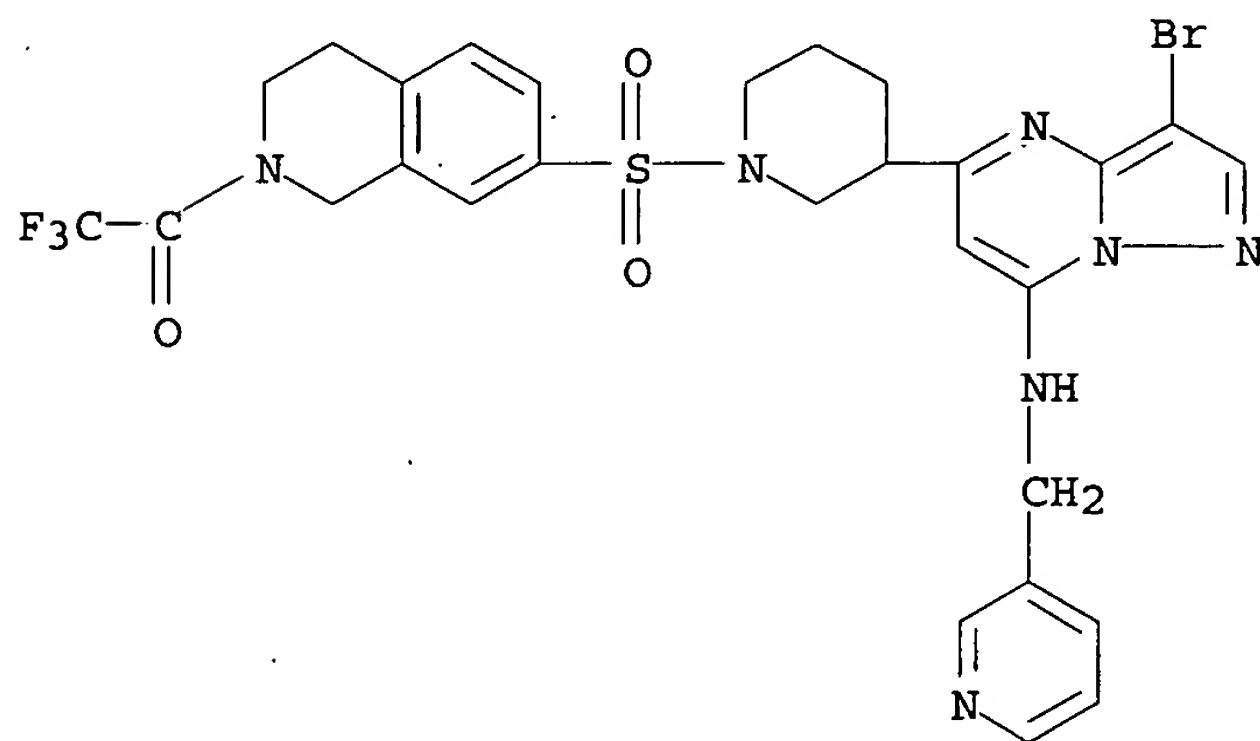


RN 677794-51-3 HCAPLUS  
 CN Piperidine, 3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-[(2,4,6-trichlorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



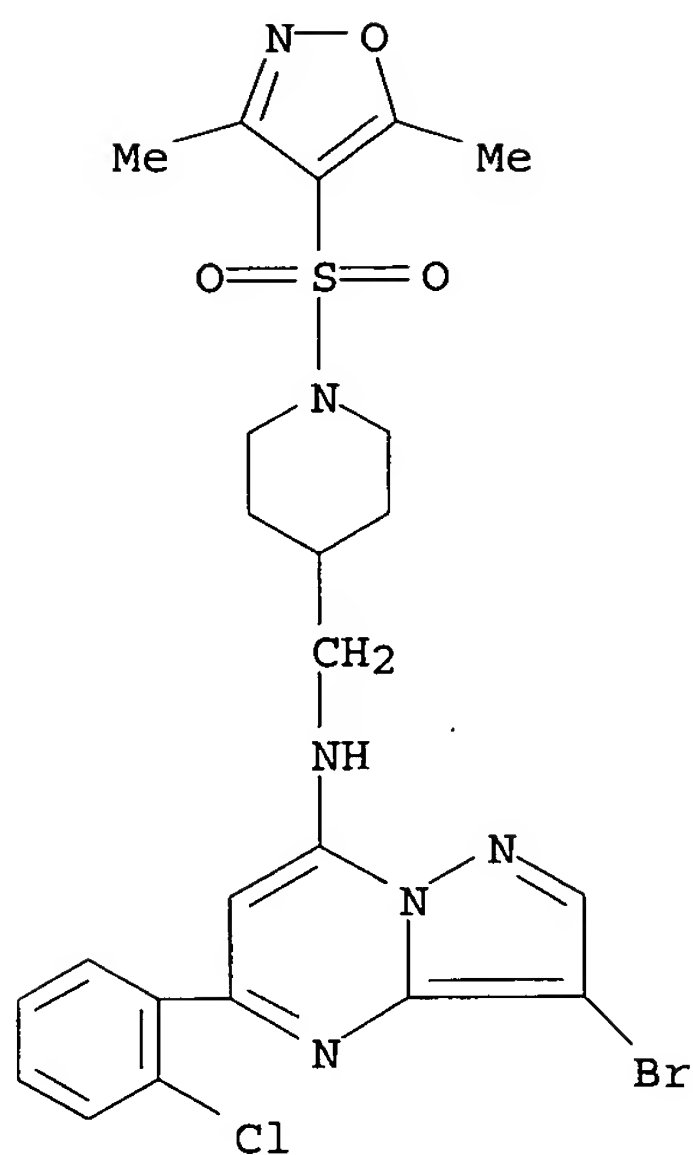
RN 677794-52-4 HCAPLUS

CN Isoquinoline, 7-[[3-[3-bromo-7-[(3-pyridinylmethyl)amino]pyrazolo[1,5-a]pyrimidin-5-yl]-1-piperidinyl]sulfonyl]-1,2,3,4-tetrahydro-2-(trifluoroacetyl)-(9CI) (CA INDEX NAME)



RN 677795-96-9 HCAPLUS

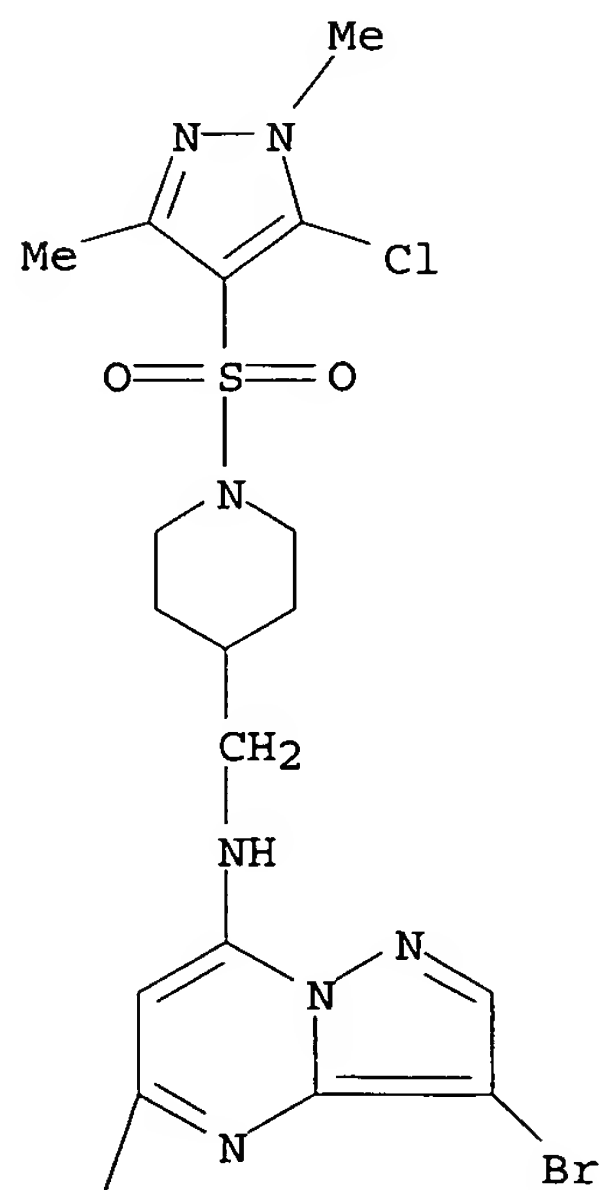
CN 4-Piperidinemethanamine, N-[3-bromo-5-(2-chlorophenyl)pyrazolo[1,5-a]pyrimidin-7-yl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-(9CI) (CA INDEX NAME)



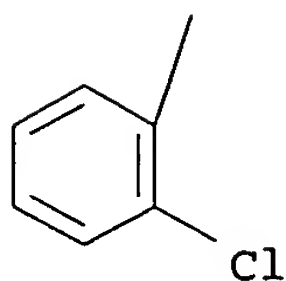
RN 677796-21-3 HCAPLUS

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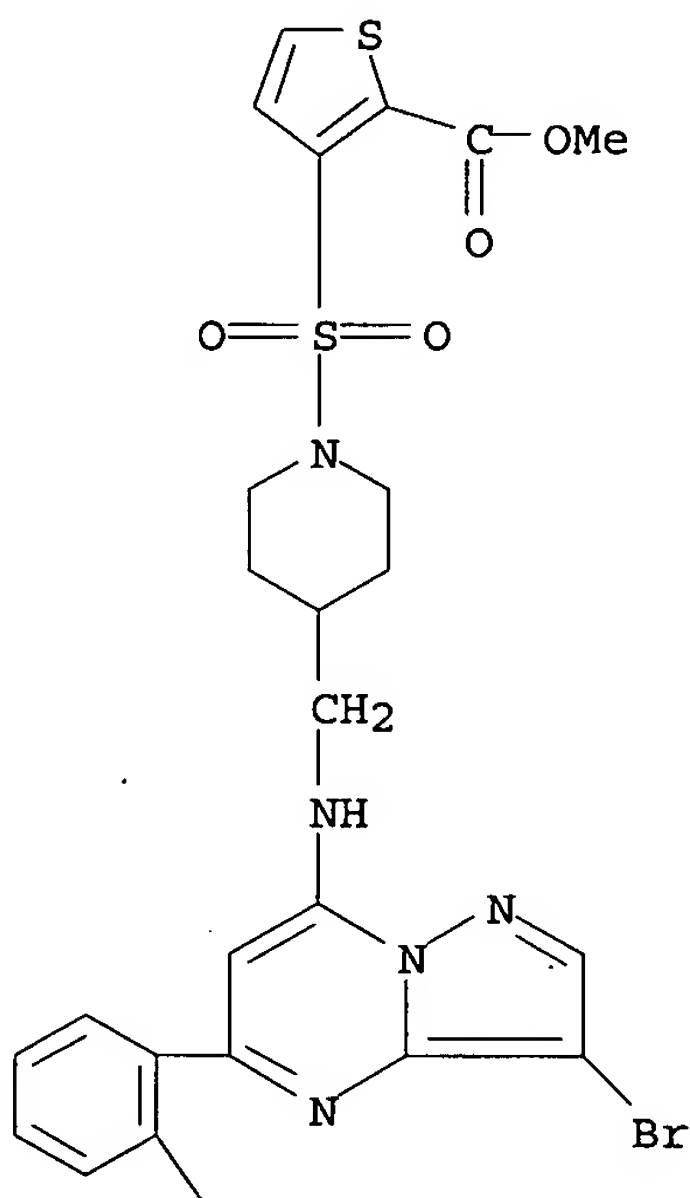


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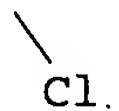


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L37 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1997:613831 HCAPLUS  
 DOCUMENT NUMBER: 127:278203  
 TITLE: Benzoxazinone and benzopyrimidinone piperidinyl  
 tocolytic oxytocin receptor antagonists  
 INVENTOR(S): Bock, Mark G.; Evans, Ben E.; Williams, Peter D.;  
 Freidinger, Roger M.; Pettibone, Douglas J.;  
 Hobbs, Doug W.; Anderson, Paul S.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA  
 SOURCE: U.S., 140 pp., Cont.-in-part of U.S. Ser. No. 92,840,  
 abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5665719	A	19970909	US 1995-470693	19950606
PRIORITY APPLN. INFO.:			US 1993-92840	B2 19930716
OTHER SOURCE(S):	MARPAT 127:278203			

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Compds. of formula I [X = O, NH, or NR<sub>8</sub>; Y = CH<sub>2</sub>, CHR<sub>8</sub>, or C(R<sub>8</sub>)<sub>2</sub>; R<sub>1</sub> = camphor-10-yl, alkoxy, styryl, hydroxystyryl, furyl, (un)substituted thienyl, naphthyl, indolyl, tetrahydronaphthyl, (un)substituted pyridyl, pyrazinyl, (un)substituted cyclohexyl or Ph; R<sub>2</sub> = H, alkoxy, alkyl, amino, alkylcarbonylamino, nitro, or halo; R<sub>3</sub> = H, alkoxycarbonyl, cyano, or carbamoyl; and m = 0 or 1] and various analogs are disclosed. The compds. as useful as oxytocin (OT) and vasopressin receptor antagonists. Over 275 synthetic examples are given. For instance, Me 2,4-dihydroxybenzoate underwent Mitsunobu etherification with N-(tert-butoxycarbonyl)-4-piperidinol (51%), followed by O-methylation of the remaining hydroxyl (88%), saponification of the Me ester (95%), and coupling of the resultant acid with 1-(4-piperidinyl)-1,2-dihydro-4H-3,1-benzoxazin-2-one (HCl salt) using EDC and HOBt (88%), to give title compound II [R = CO<sub>2</sub>Bu-tert]. The latter was deprotected with HCl in dioxane (93%) and acetylated with Ac<sub>2</sub>O (89%) to give title compound II [R = Ac]. The latter inhibited binding of [3H]-OT to rat uterine OT receptors in vitro with an IC<sub>50</sub> of 47 nM.

IT 162043-19-8P 162044-15-7P

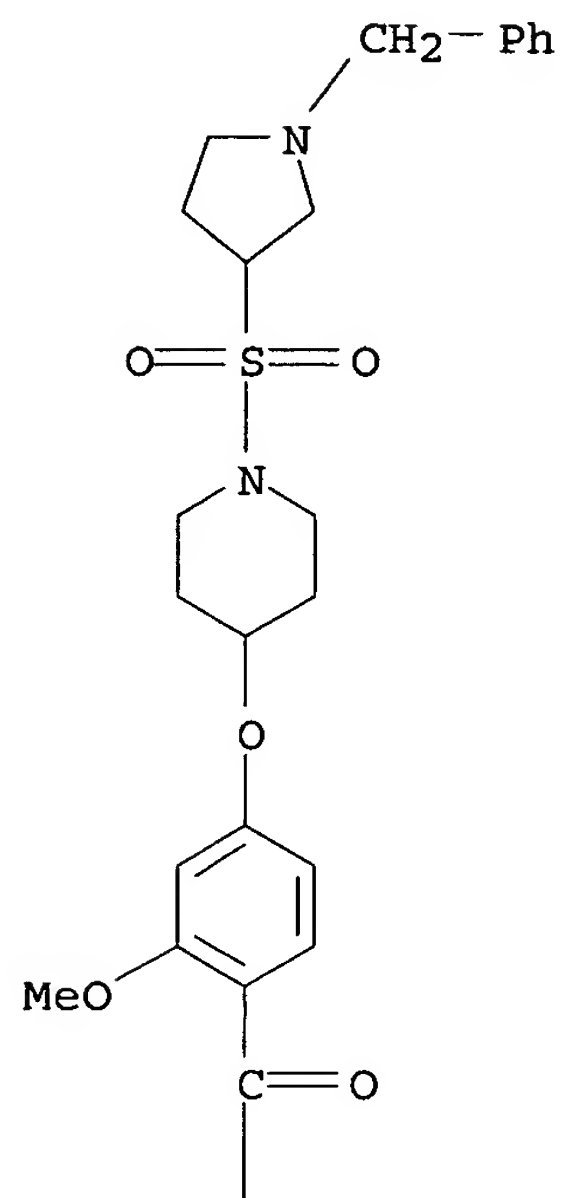
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(preparation of benzoxazinone and benzopyrimidinone derivs. as oxytocin and vasopressin receptor antagonists)

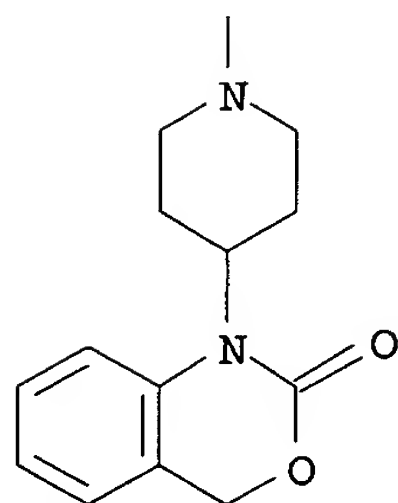
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 (CA INDEX NAME)

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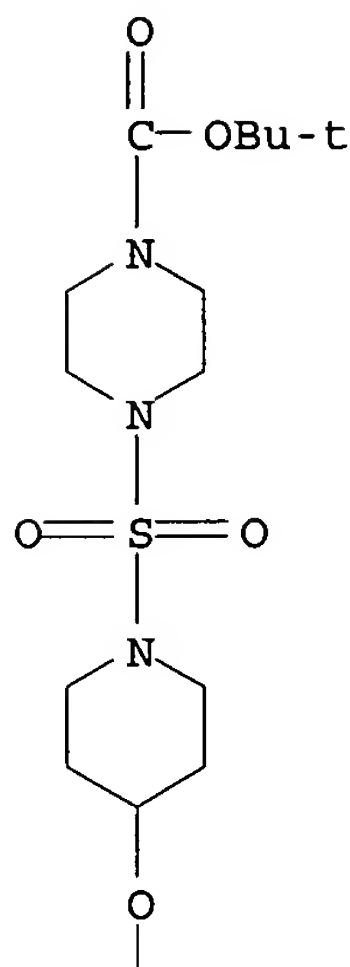


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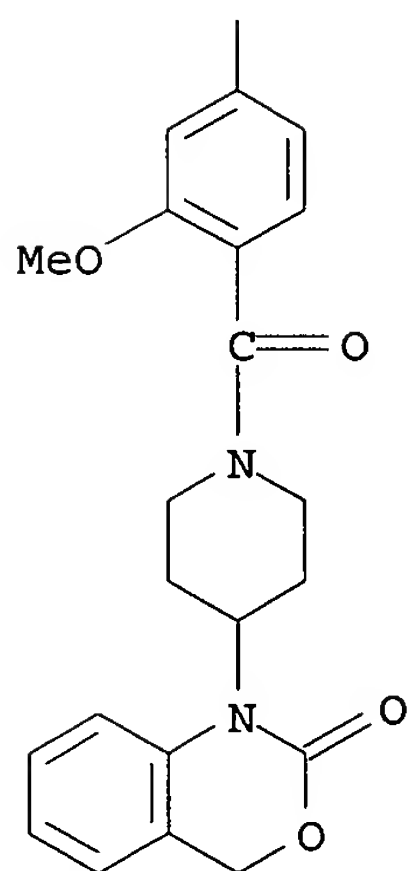


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IT 162043-21-2P 162044-10-2P 162044-11-3P  
162044-17-9P 162044-18-0P 162044-19-1P  
196793-98-3P 196794-19-1P 196794-20-4P  
196794-23-7P 196794-24-8P 196794-25-9P

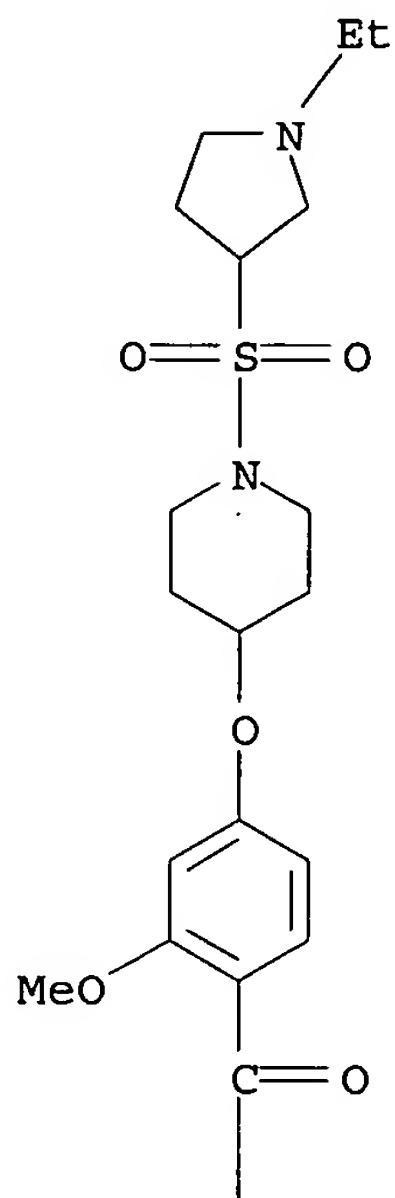
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(preparation of benzoxazinone and benzopyrimidinone derivs. as oxytocin and vasopressin receptor antagonists)

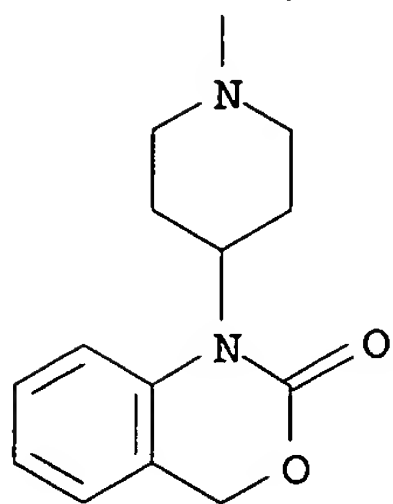


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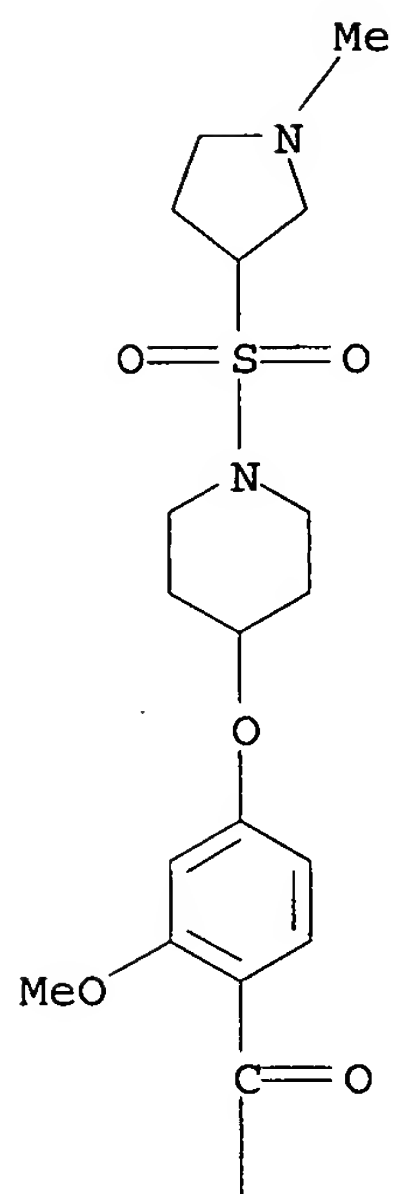
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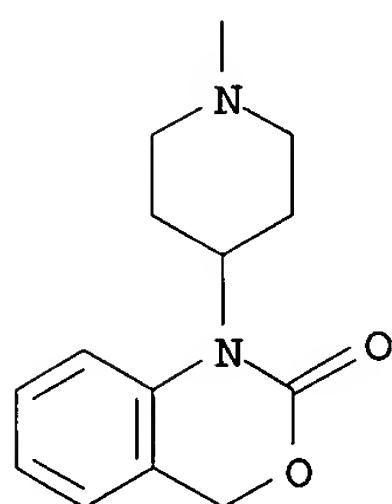
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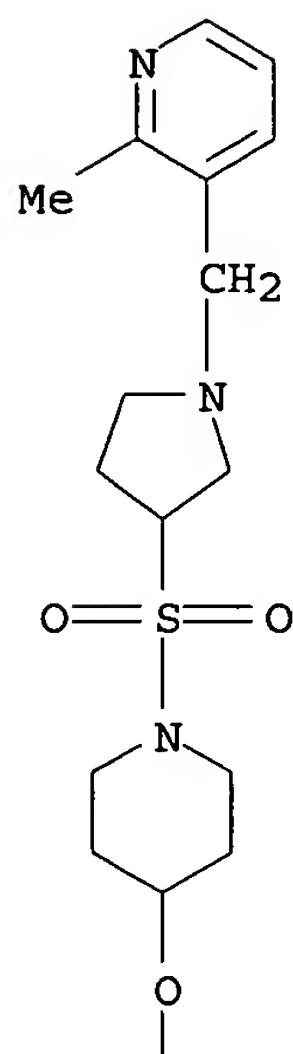
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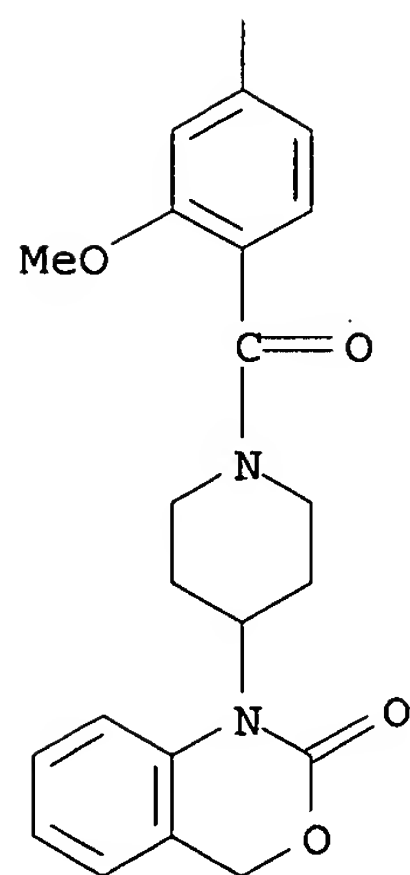
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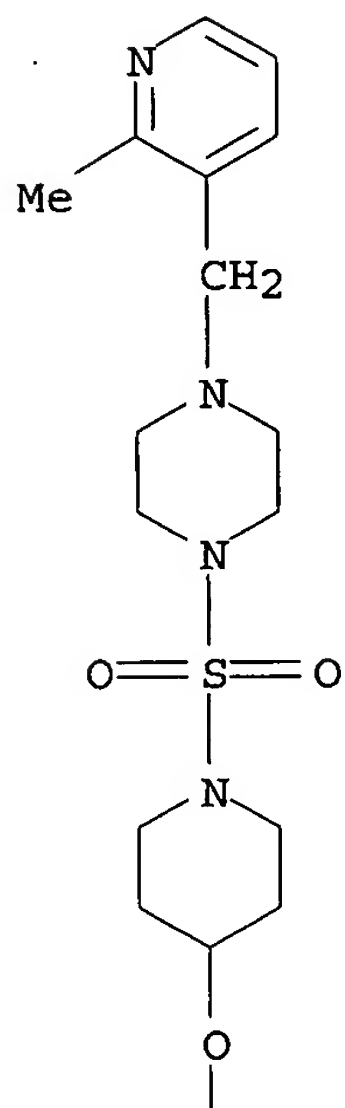
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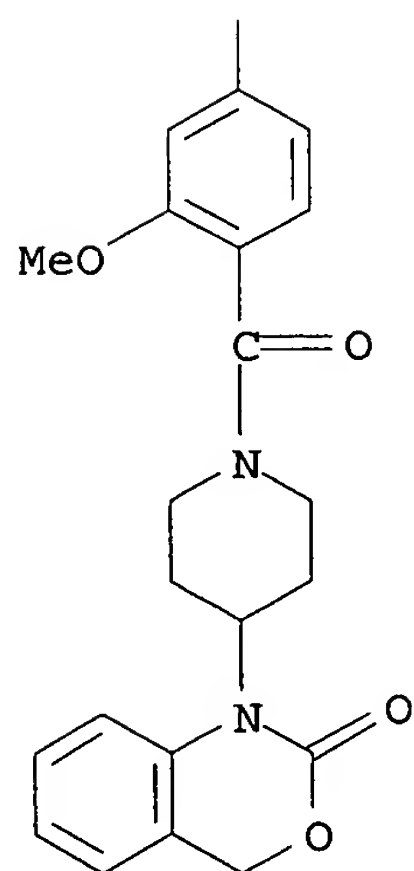
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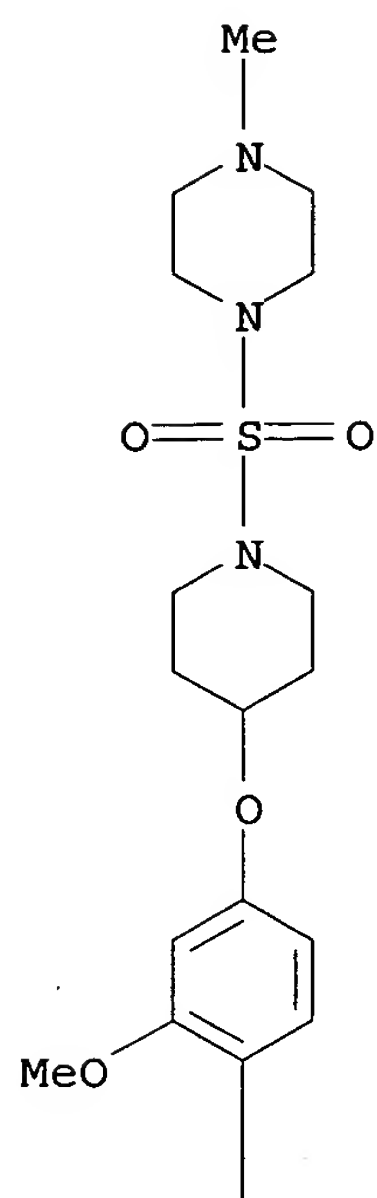
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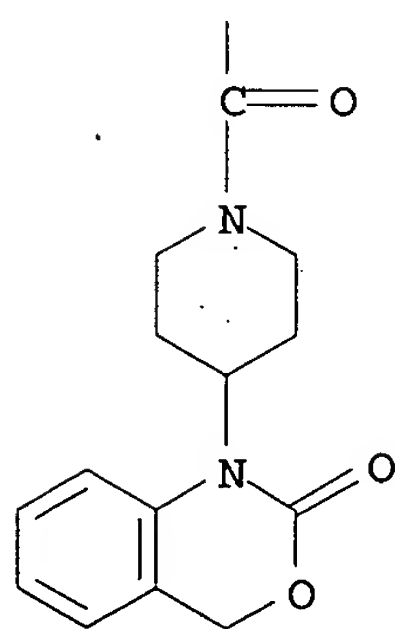
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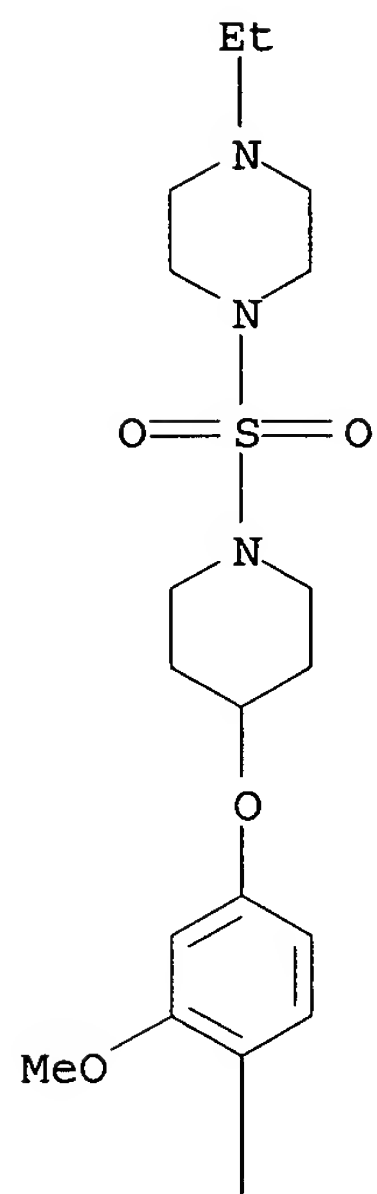
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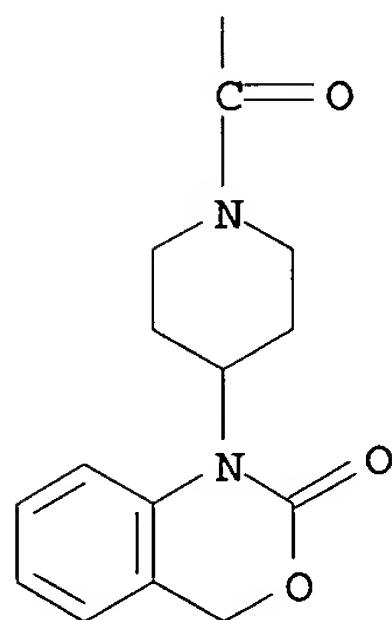
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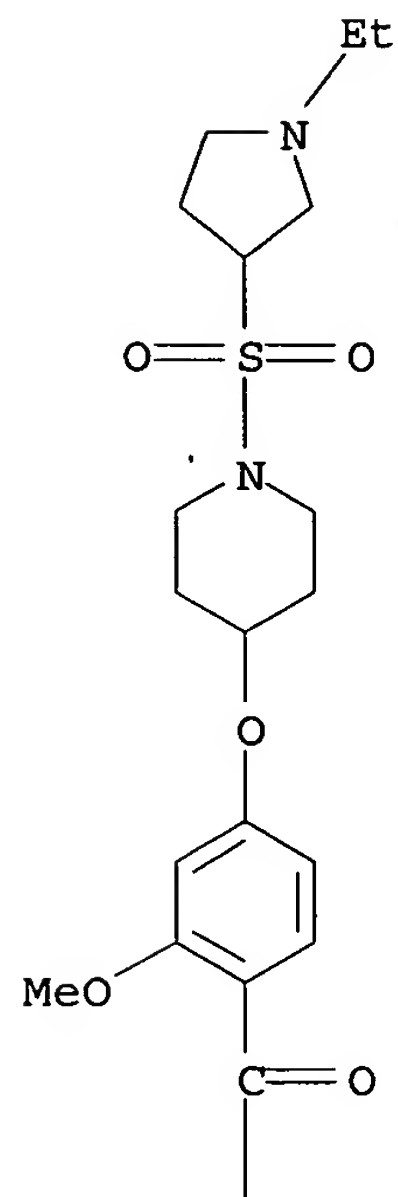
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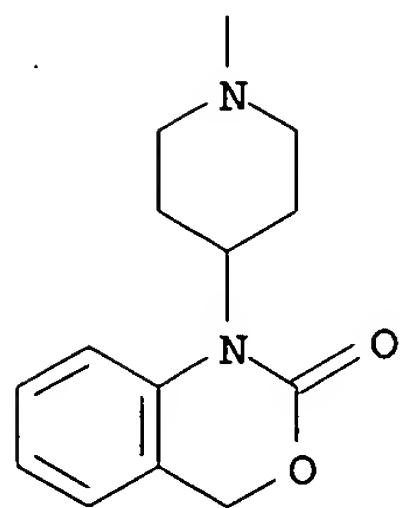
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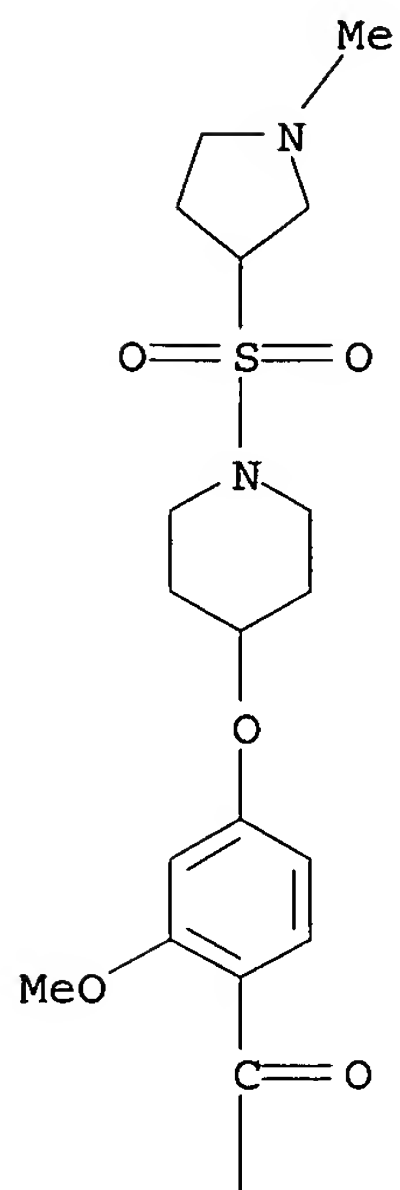


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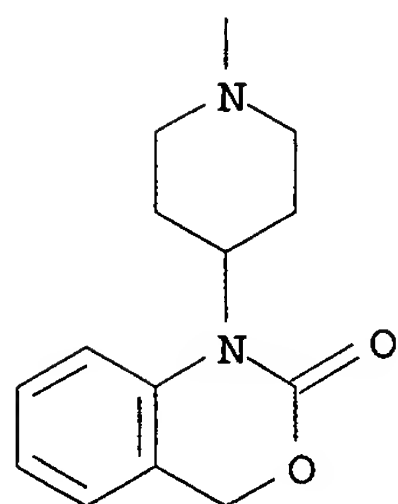


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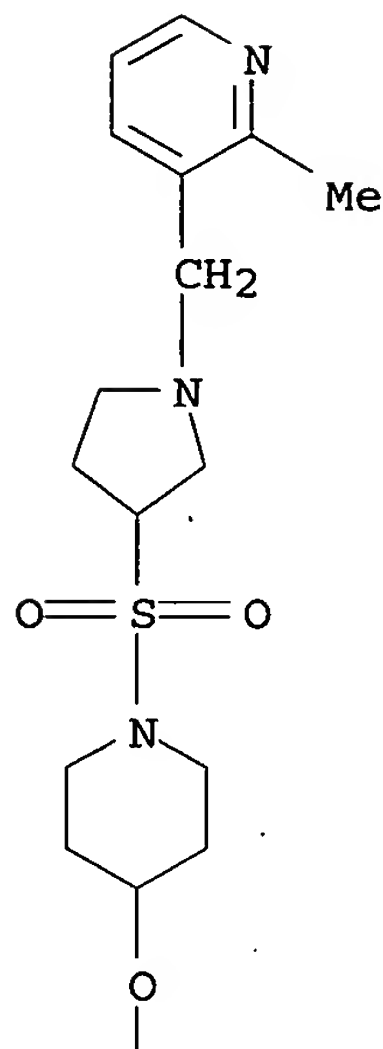
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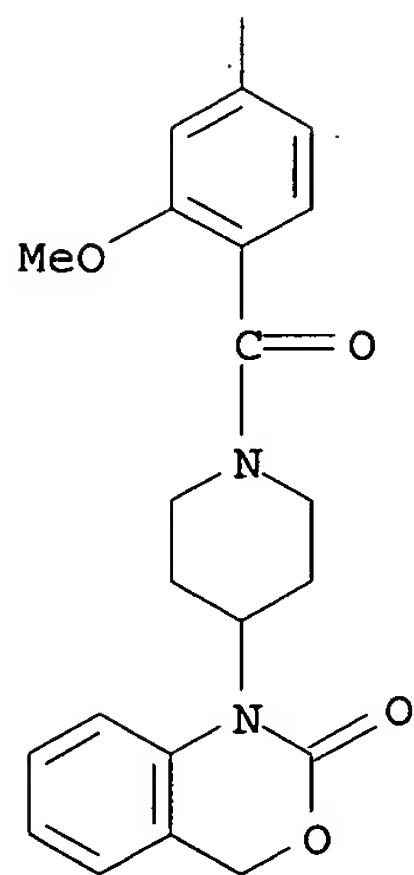
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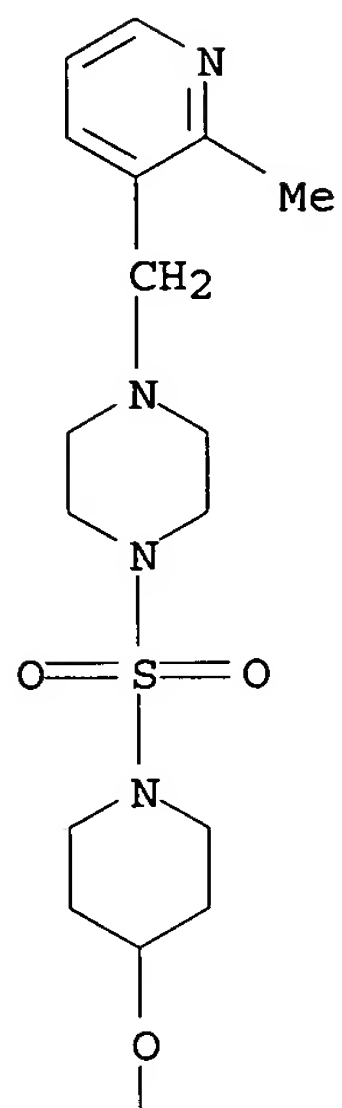


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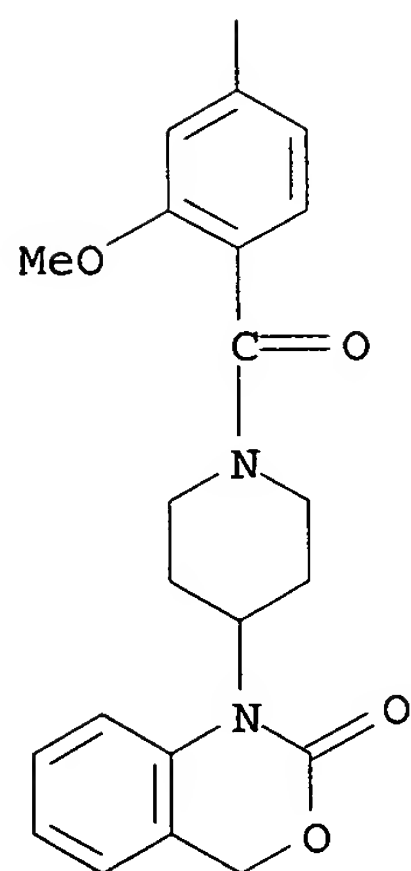


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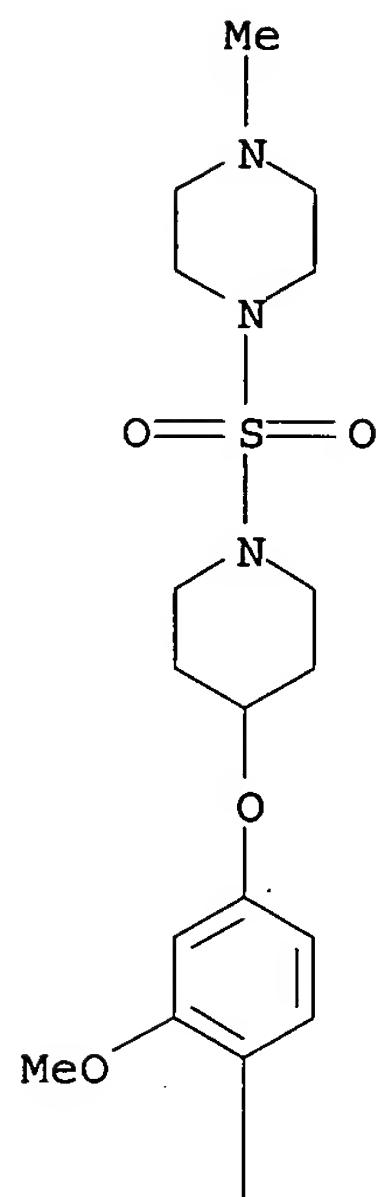


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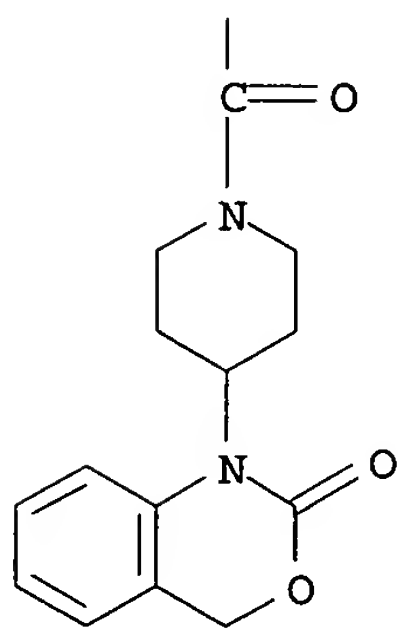


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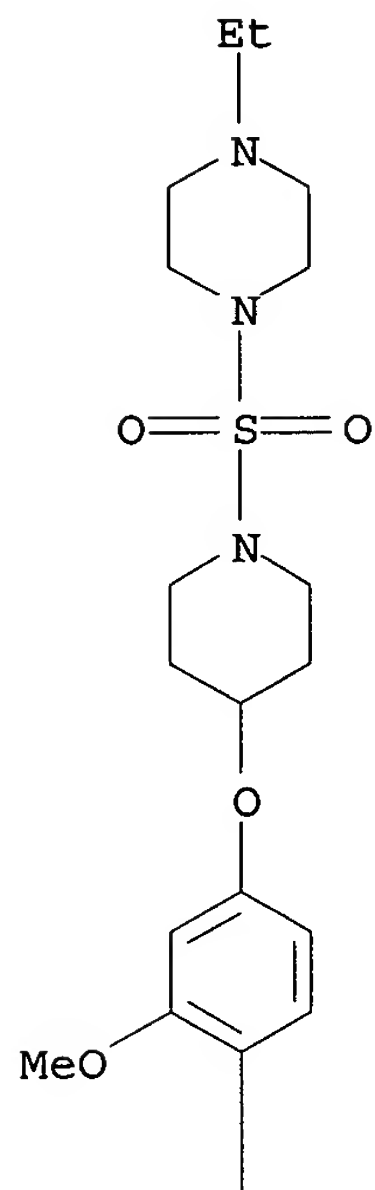


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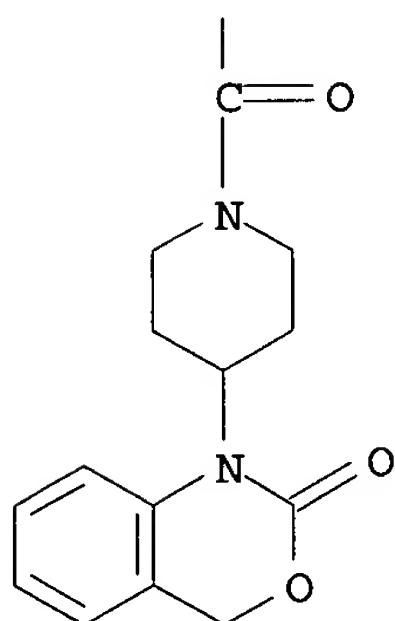


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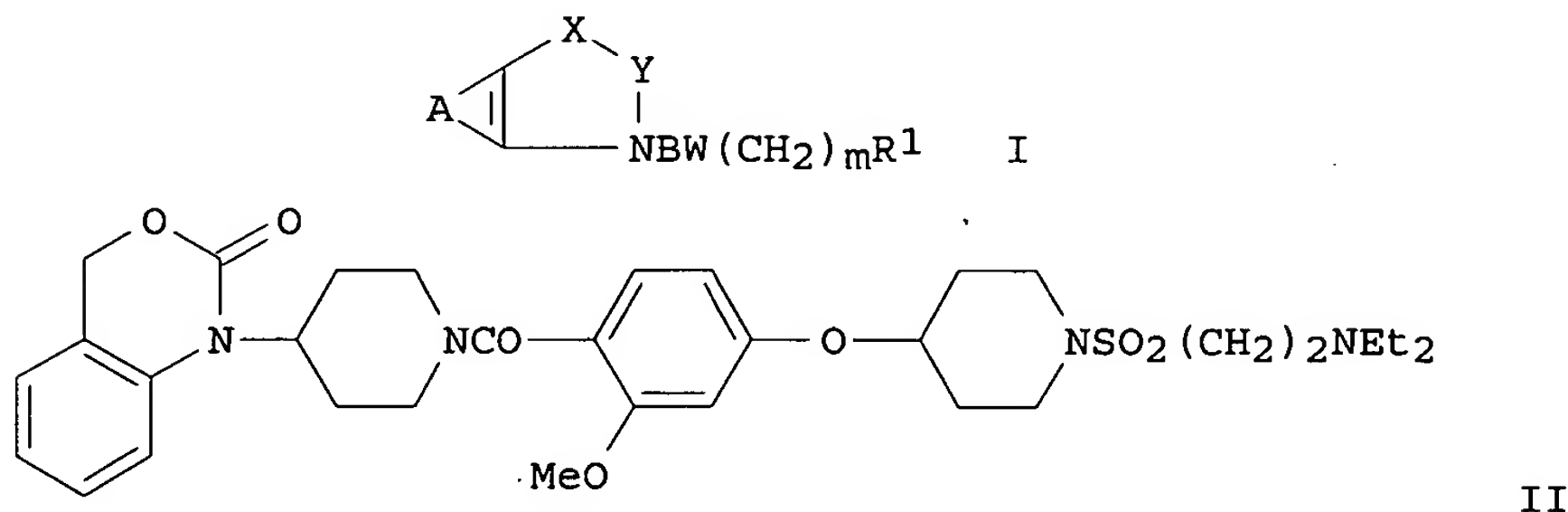
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L37 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1995:470323 HCAPLUS  
 DOCUMENT NUMBER: 123:276051  
 TITLE: Benzoxazinone and benzopyrimidinone piperidinyl  
 tocolytic oxytocin receptor antagonists  
 INVENTOR(S): Bock, Mark G.; Evans, Ben E.; **Hobbs, Doug W.**  
 ; Williams, Peter D.; Anderson, Paul S.; Freidinger,  
 Roger M.; Pettibone, Douglas J.  
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA  
 SOURCE: PCT Int. Appl., 385 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

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PRIORITY APPLN. INFO.:			US 1993-92840	A 19930716
			WO 1994-US7784	W 19940714
OTHER SOURCE(S):		MARPAT 123:276051		
GI				



AB Fused N-containing heterocyclic ring system derivs. I [A completes a 5- or 6-membered carbocyclic or N- and/or S-containing heterocyclic ring; X = O, NH, (CH<sub>2</sub>)<sub>q</sub>O, CH<sub>2</sub>NH, OCH<sub>2</sub>, CH:CH, S, etc.; Y = CH<sub>2</sub>, C:O, C:S, C:NH, C:NMe; B = (substituted) N-containing heterocyclic or heterobicyclic ring; W = CH<sub>2</sub>, C:O, CO<sub>2</sub>, SO<sub>2</sub>, C(:NCH<sub>2</sub>Ph), etc.; R<sub>1</sub> = (hetero)aryl, C1-5 alkoxy, camphor-10-yl] are useful as oxytocin and vasopressin receptor antagonists, e.g in treatment of preterm labor and dysmenorrhea and in stopping labor preparatory to cesarean delivery. Thus, in competitive radioligand binding assays on rat uterus membrane preps., high-affinity binding of oxytocin-3H was inhibited by 1-[1-[4-[1-[(diethylaminoethyl)sulfonyl]-4-piperidinyloxy]-2-methoxybenzoyl]piperidin-4-yl]-1,2-dihydro-4H-3,1-benzoxazin-2-one (II) with an IC<sub>50</sub> of 23 nM. II was prepared in 7 steps from Me 2,4-dihydroxybenzoate, N-tert-butyloxy-4-piperidinol, 1-(4-piperidinyl)-1,2-dihydro-4H-3,1-benzoxazin-2-one-HCl (preparation given), ClCH<sub>2</sub>CH<sub>2</sub>SO<sub>2</sub>Cl, and HNEt<sub>2</sub>. Preparation of 277 compds. of formula I is described.

IT 162043-19-8P 162043-21-2P 162044-10-2P  
162044-11-3P 162044-15-7P 162044-17-9P

162044-18-0P 162044-19-1P

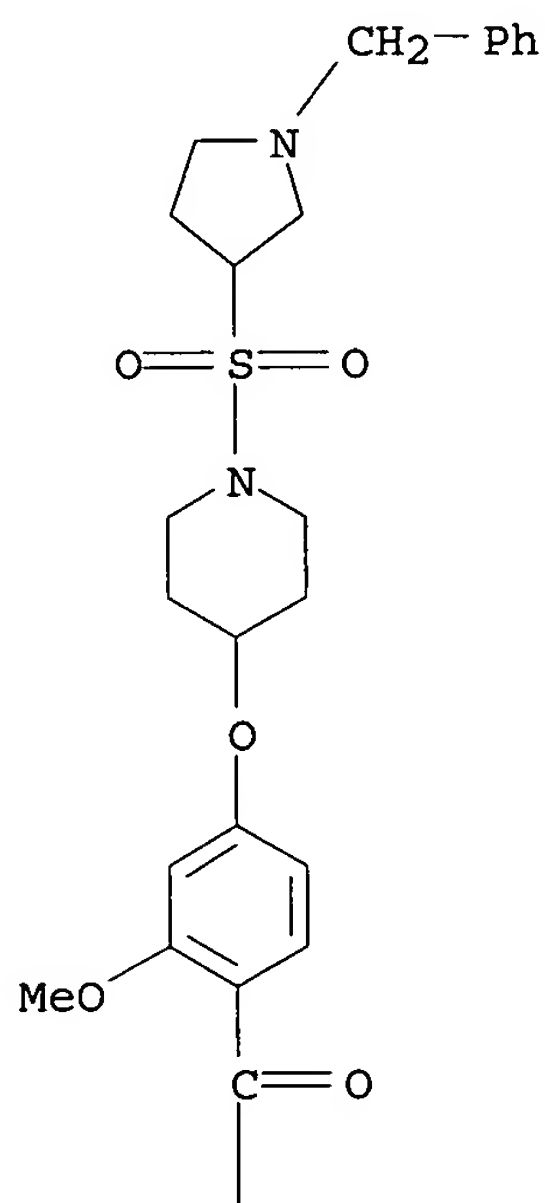
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(benzoxazinone and benzopyrimidinone piperidinyl tocolytic oxytocin receptor antagonists)

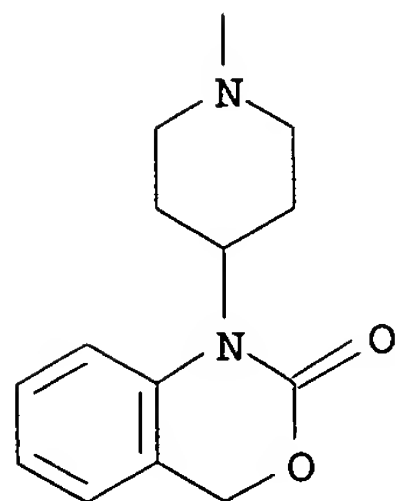
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(CA INDEX NAME)

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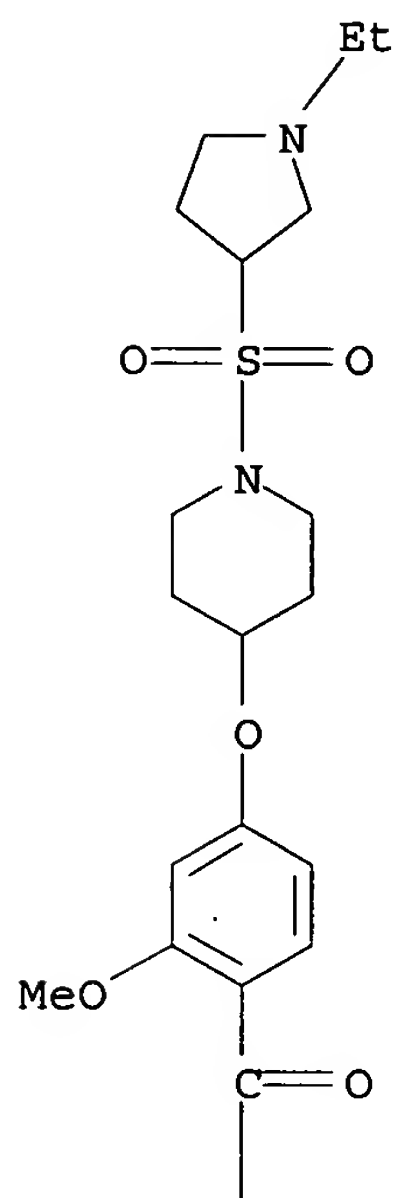
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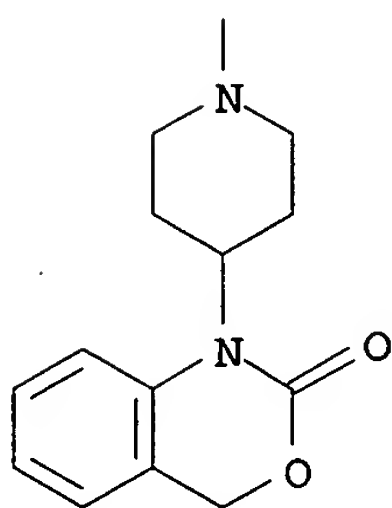
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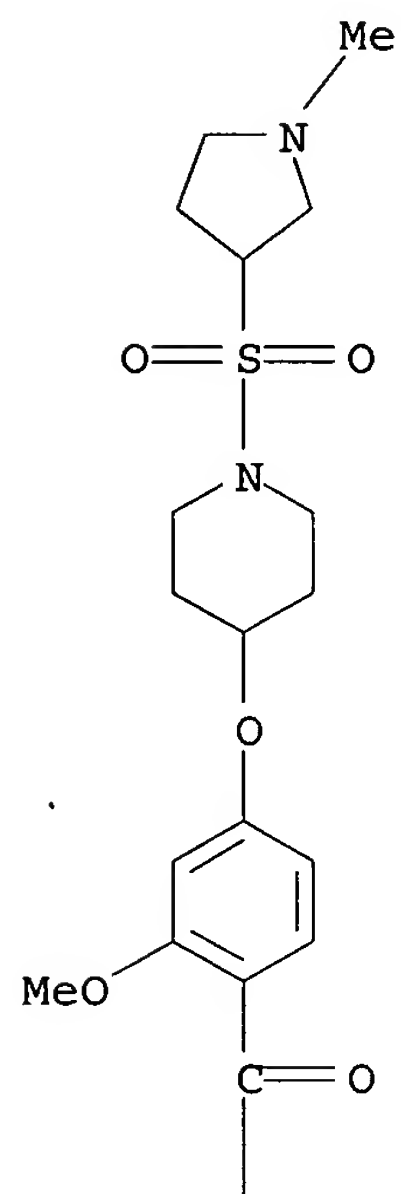
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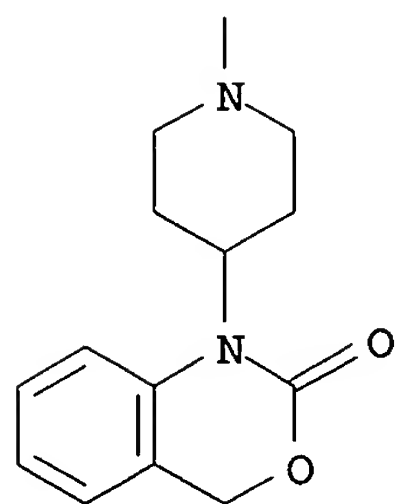
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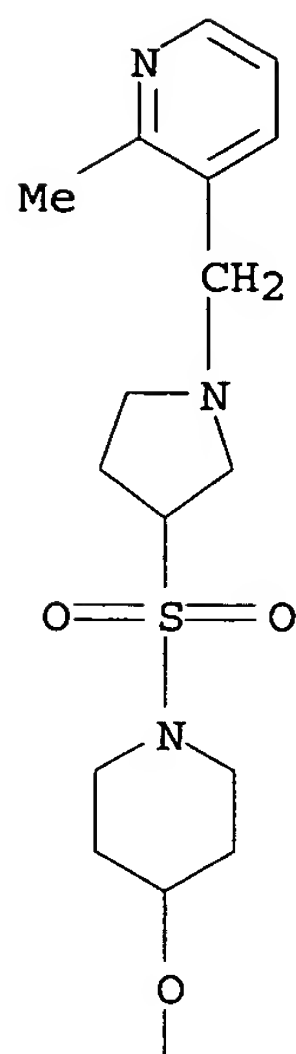


● HCl

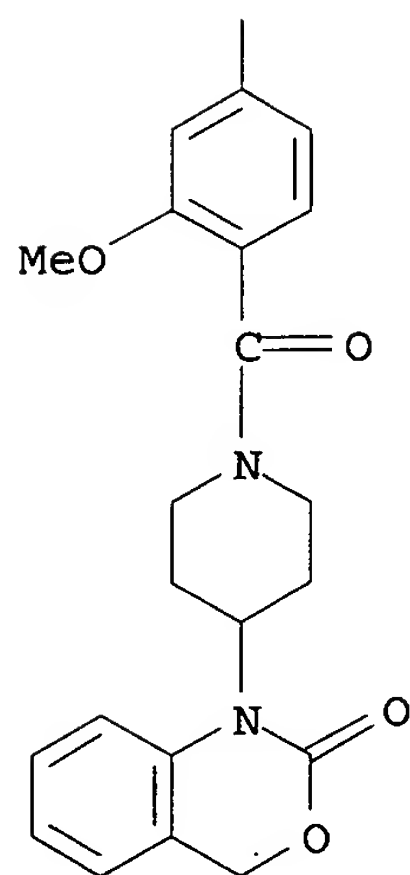
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PAGE 1-A



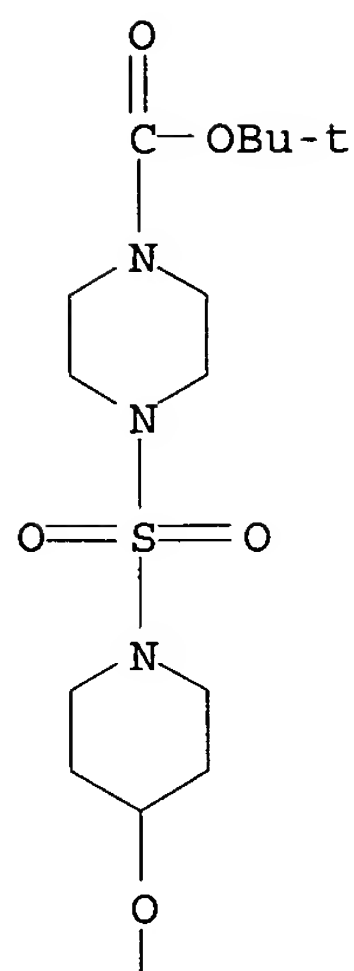
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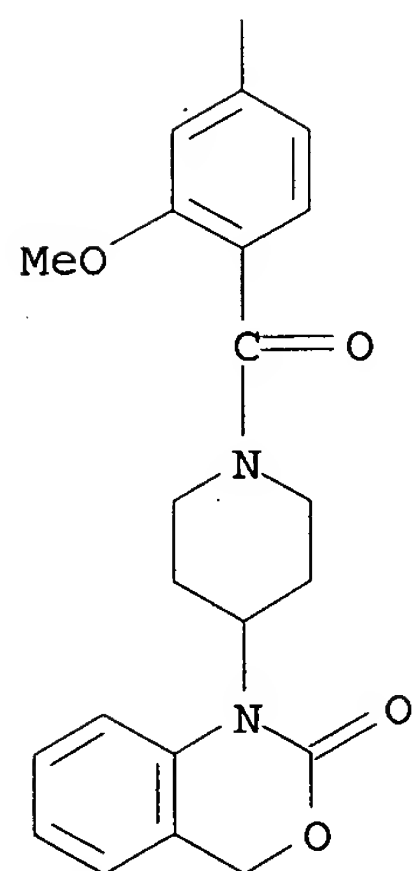
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RN 162044-15-7 HCAPLUS  
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PAGE 1-A

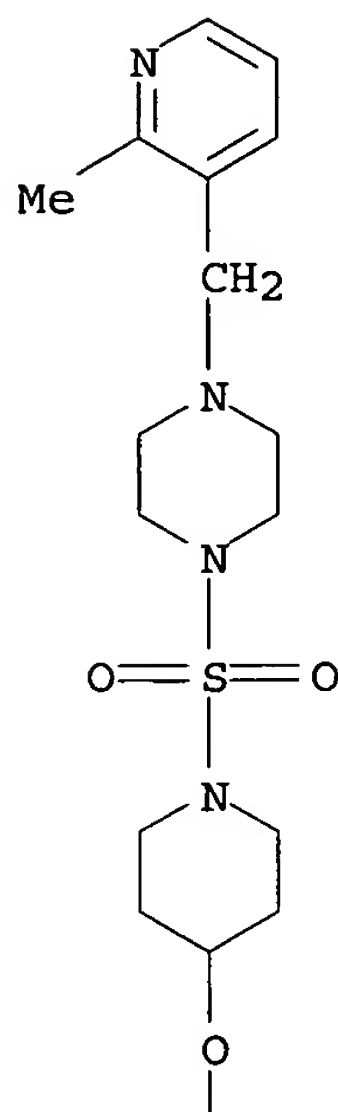


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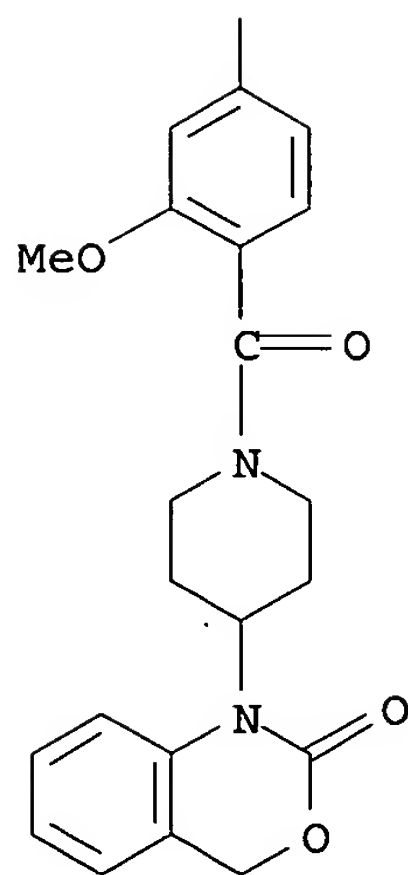


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PAGE 1-A



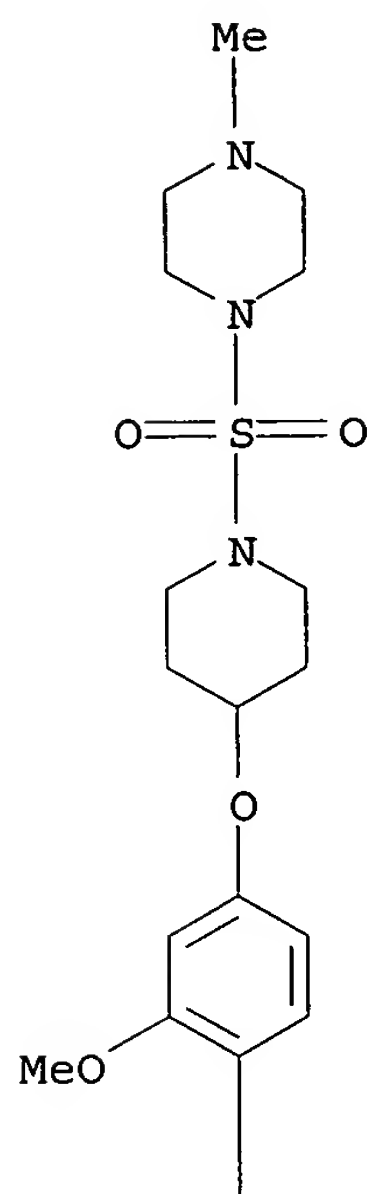
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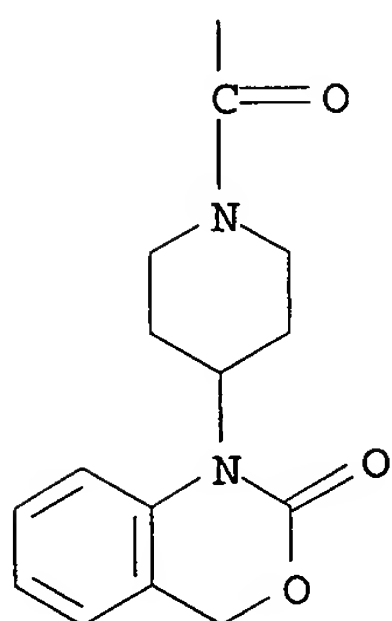
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PAGE 1-A



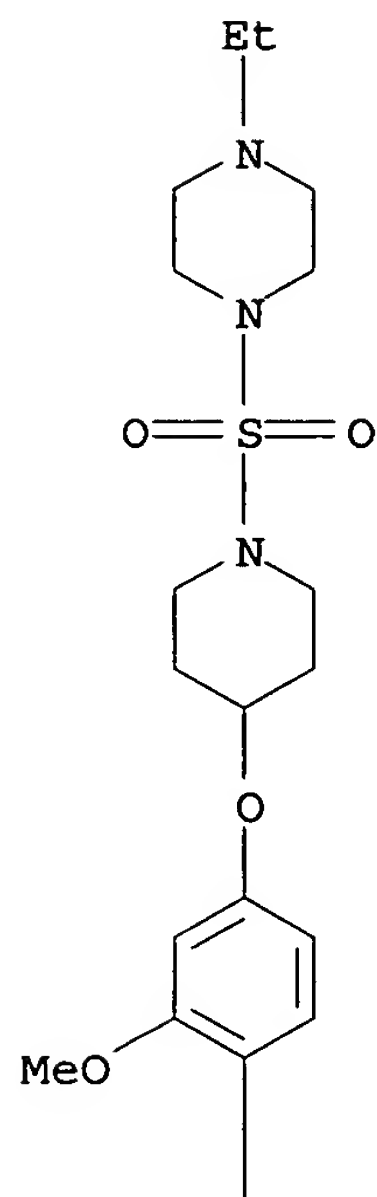
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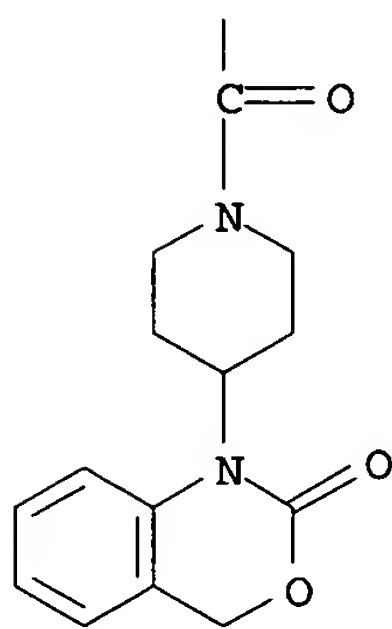
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RN 162044-19-1 HCAPLUS  
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PAGE 1-A



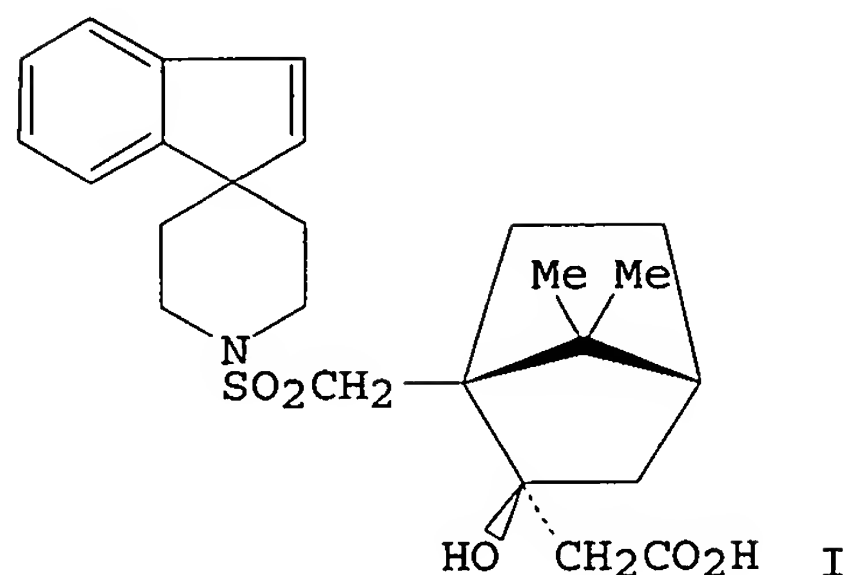
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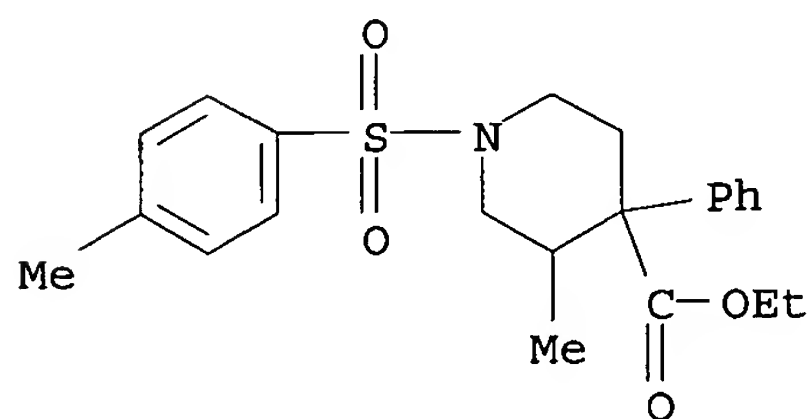
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L37 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1992:591648 HCAPLUS  
DOCUMENT NUMBER: 117:191648  
TITLE: Orally active, nonpeptide oxytocin antagonists  
AUTHOR(S): Evans, Ben E.; Leighton, James L.; Rittle, Kenneth E.;  
Gilbert, Kevin F.; Lundell, George F.; Gould, Norman  
P.; Hobbs, Doug W.; DiPardo, Robert M.;  
Veber, Daniel F.; et al.  
CORPORATE SOURCE: Dep. Med. Chem., Merck Res. Lab., West Point, PA,

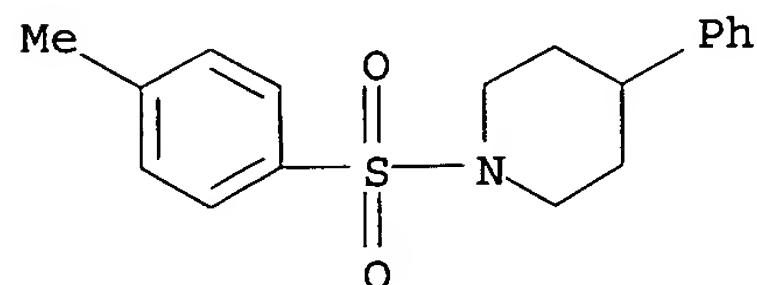
SOURCE: 19486, USA  
Journal of Medicinal Chemistry (1992), 35(21), 3919-27  
CODEN: JMCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



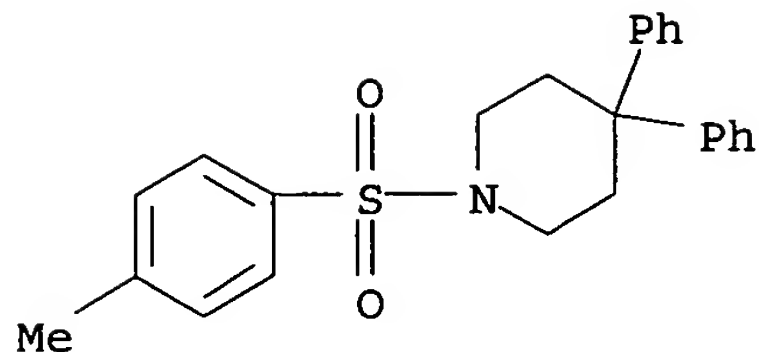
AB Spiroindene-piperidines, including I, were prepared as orally bioavailable oxytocin antagonists; I showed good in vivo duration. The potential use of these agents for treatment of preterm labor and their significance as new nonpeptide ligands for peptide receptors are discussed.  
IT 95941-26-7P 143632-57-9P 143632-58-0P  
143632-60-4P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and oxytocin antagonist activity of)  
RN 95941-26-7 HCAPLUS  
CN 4-Piperidinecarboxylic acid, 3-methyl-1-[(4-methylphenyl)sulfonyl]-4-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 143632-57-9 HCAPLUS  
CN Piperidine, 1-[(4-methylphenyl)sulfonyl]-4-phenyl- (9CI) (CA INDEX NAME)

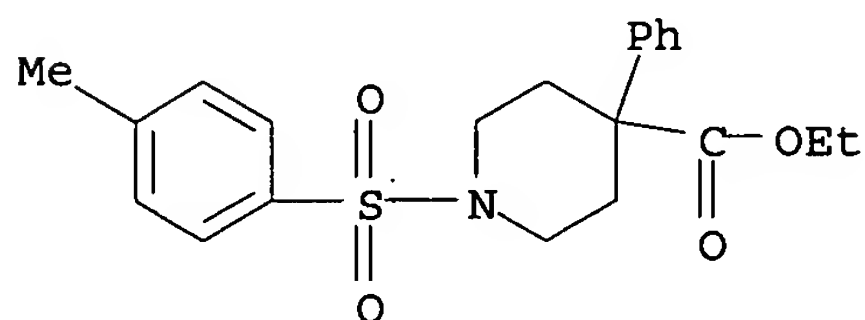


RN 143632-58-0 HCAPLUS  
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RN 143632-60-4 HCAPLUS

CN 4-Piperidinecarboxylic acid, 1-[(4-methylphenyl)sulfonyl]-4-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



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 L10 STR  
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 L13 STR  
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 L18 183 SEA FILE=REGISTRY ABB=ON PLU=ON SECRETASE  
 L19 3443 SEA FILE=HCAPLUS ABB=ON PLU=ON L17  
 L20 2011 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR ?SECRETASE?  
 L21 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND L20  
 L22 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 NOT L16  
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 L36 85 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOBBS D"/AU OR "HOBBS D W"/AU OR ("HOBBS DOUG W"/AU OR "HOBBS DOUGLAS"/AU) OR ("HOBBS DOUGLAS W"/AU OR "HOBBS DOUGLAS WALSH"/AU)) NOT (L16 OR L22 OR L32 OR L34 OR L35)  
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Ward 10\_663042-inventor search

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L35 27 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ASBEROM T"/AU OR "ASBEROM  
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L37 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L36 AND L19  
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L4 STR  
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L29 78 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND ENZYME(L) INHIBIT?



Ward 10\_663042-inventor search

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 OR L22 OR L32)  
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 W"/AU OR ("HOBBS DOUG W"/AU OR "HOBBS DOUGLAS"/AU) OR ("HOBBS  
 DOUGLAS W"/AU OR "HOBBS DOUGLAS WALSH"/AU)) NOT (L16 OR L22 OR  
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 L38 100 SEA FILE=HCAPLUS ABB=ON PLU=ON "SMITH ELIZABETH"/AU OR  
 ("SMITH ELIZABETH M"/AU OR "SMITH ELIZABETH MARGERY"/AU OR  
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 L41 141 SEA FILE=HCAPLUS ABB=ON PLU=ON "GUO TAO"/AU  
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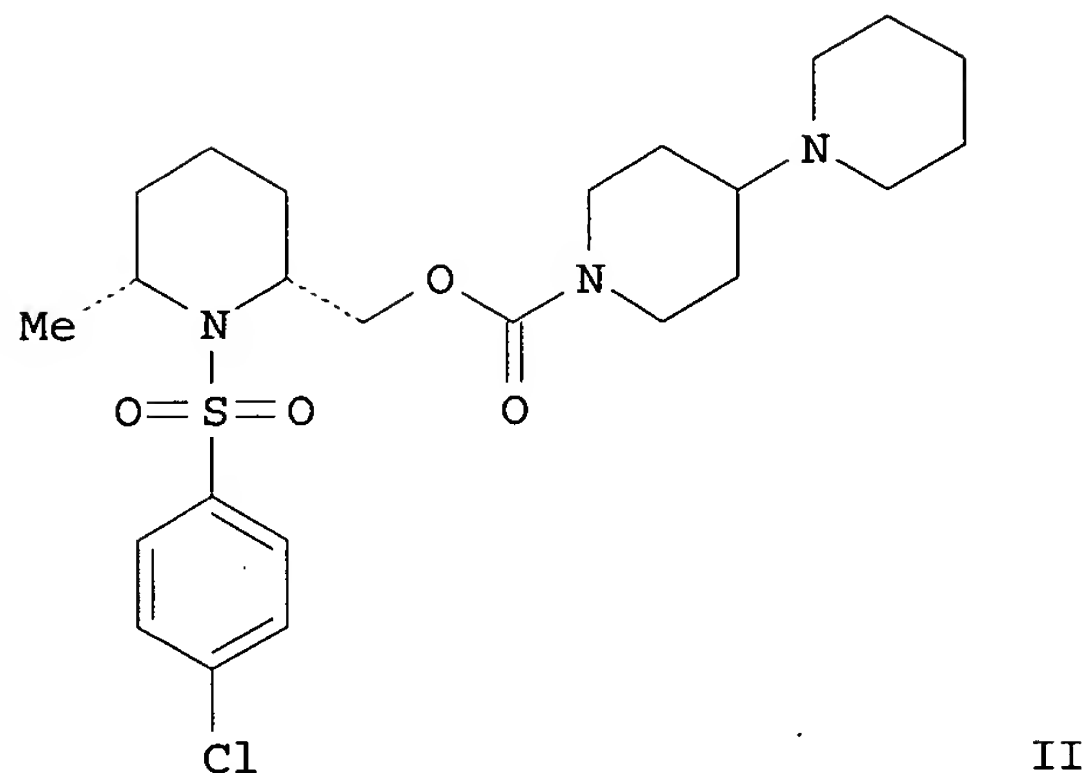
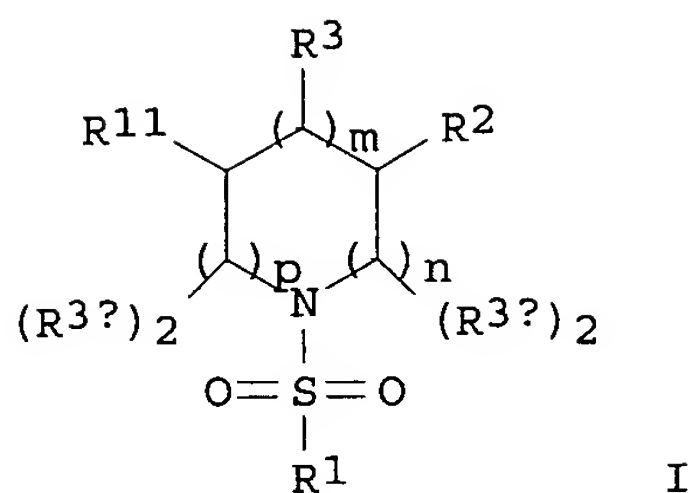
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L43 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2005:346733 HCAPLUS  
 TITLE: Preparation of 1-(arylsulfonyl)piperidines as  
 $\gamma$ -secretase inhibitors for treatment of  
 neurodegenerative diseases  
 INVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,  
 Elizabeth M.; Clader, John W.; Asberom, Theodros;  
 Guo, Tao; Hobbs, Douglas W.  
 PATENT ASSIGNEE(S): Schering-Plough Corp., USA; Pharmacoepia,  
 Inc.  
 SOURCE: U.S. Pat. Appl. Publ., 170 pp., Cont.-in-part of U.S.  
 Ser. No. 663,042.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005085506	A1	20050421	US 2004-941440	20040915
US 2004048848	A1	20040311	US 2003-358898	20030205
US 2004171614	A1	20040902	US 2003-663042	20030916
PRIORITY APPLN. INFO.:			US 2002-355618P	P 20020206
			US 2003-358898	A2 20030205
			US 2003-663042	A2 20030916

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AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un)substituted (hetero)aryl, etc.; R3 = H, alkyl, OH, alkoxy, etc.; R3a, R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as  $\gamma$ -secretase inhibitors, which inhibit the deposition of  $\beta$ -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K<sub>2</sub>CO<sub>3</sub>. The aldehyde was converted to the alc. with NaBH<sub>4</sub> and protected with t-BuPh<sub>2</sub>SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchlorocarbonate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited  $\gamma$ -secretase activity in transfected human APP cells with an IC<sub>50</sub> value in the range of about 0.0002  $\mu$ M to about 15  $\mu$ M. Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

L43 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:158632 HCAPLUS

DOCUMENT NUMBER: 142:261556

TITLE: Preparation of aminohydroxyalkyl cyclic amine BACE-1 inhibitors having a benzamide substituent

INVENTOR(S): Cumming, Jared N.; Iserloh, Ulrich; Stamford, Andrew; Strickland, Corey; Voigt, Johannes H.; Wu, Yusheng; Huang, Ying; Xia, Yan; Chackalamannil, Samuel; Guo, Tao; Hobbs, Douglas W.; Le, Thuy X. H.; Lowrie, Jeffrey F.; Saionz, Kurt W.; Babu, Suresh D.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug  
Discovery, Inc  
SOURCE: PCT Int. Appl., 118 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016876	A2	20050224	WO 2004-US25018	20040804
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2003-493987P P 20030808  
OTHER SOURCE(S): MARPAT 142:261556  
GI

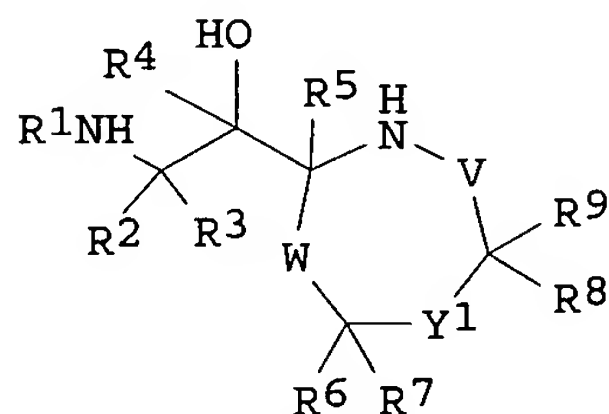
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1 = Q1, Q2, etc.; Q3 = (CR10R11)l; Q4 = (CR12R13)n; R = CONR27R28, PO(OR29)2; R2 = H, (substituted) alkyl, cycloalkyl, heterocycloalkyl, cycloalkylalkyl, aryl, heteroaryl, etc.; R3, R4 = H, (substituted) alkyl; R5 = H, (substituted) alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl; R14 = 1-4 of H, (substituted) alkyl, alkenyl, alkynyl, halo, cyano, haloalkyl, cycloalkyl, aryl, heteroaryl, etc.; R27, R28 = alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, alkoxyalkyl, etc.; NR27R28 = (substituted) 3-7 membered ring; R29 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, alkoxyalkyl, etc.; l, n = 0-3; m = 0, 1; R6-R11 = H, (substituted) alkyl, cycloalkyl, aryl, heteroaryl, aralkyl, alkenyl, alkynyl, halo, NO2, cyano, etc.; R12, R13 = H, (substituted) alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heterocycloalkyl, alkenyl, alkynyl, etc.; with provisos], were prepared  
Thus, title compound (II) (preparation outlined) inhibited a soluble human BACE-1  
with IC50 = 1.4 nM.

L43 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2005:141026 HCAPLUS  
DOCUMENT NUMBER: 142:240330  
TITLE: Preparation of cyclic amine BACE-1 inhibitors having a heterocyclic substituent  
INVENTOR(S): Cumming, Jared N.; Huang, Ying; Li, Guoqing; Iserloh, Ulrich; Stamford, Andrew; Strickland, Corey; Voigt, Johannes H.; Wu, Yusheng; Pan, Jianping; Guo, Tao; Hobbs, Douglas W.; Le, Thuy X. H.; Lowrie, Jeffrey F.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug  
Discovery, Inc.  
SOURCE: PCT Int. Appl., 127 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005014540	A1	20050217	WO 2004-US25748	20040804
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US 2005043290	A1	20050224	US 2004-911030	20040804
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OTHER SOURCE(S):	MARPAT 142:240330			
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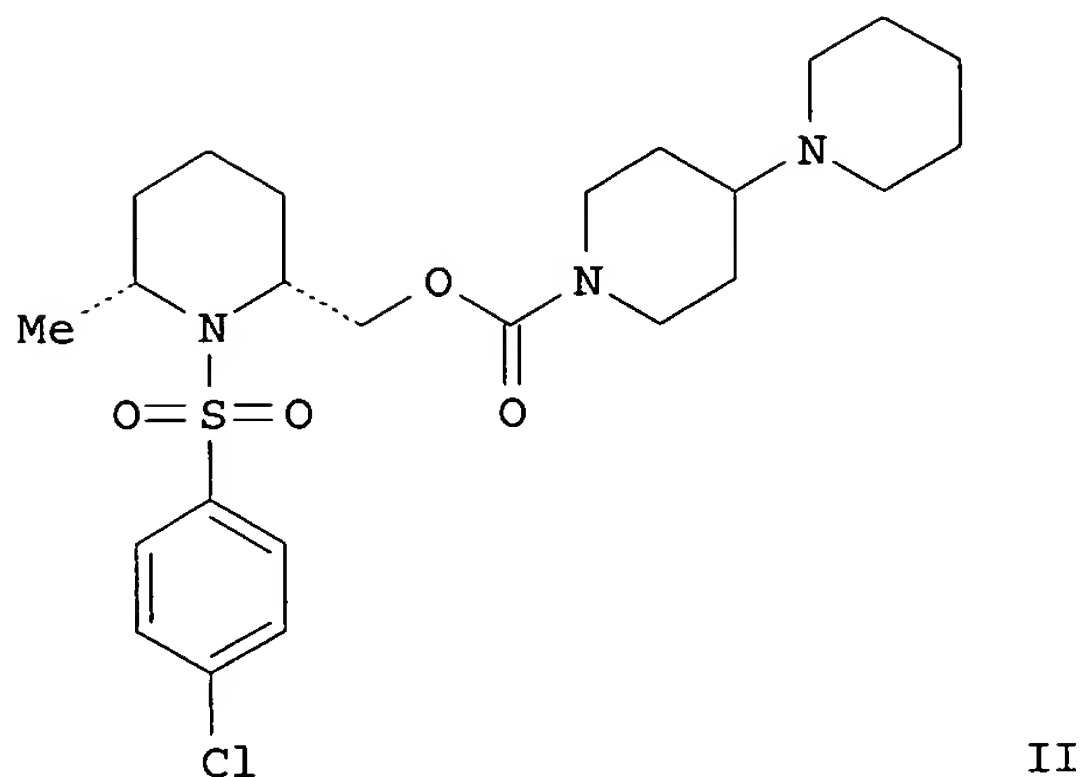
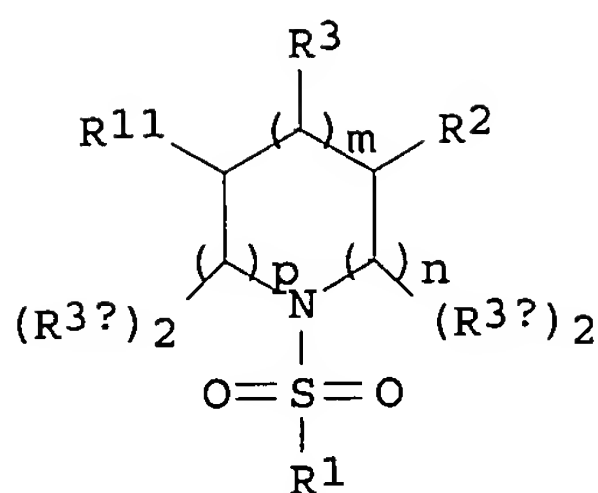
I

AB Disclosed are novel compds., e.g., I [R1 = azcycloalkylcarbamoyl, carbamoyl (from piperazine, piperidine or pyrrolidine derivs.); X = O, C(R14)2, N(R); Z is -C(R14)2- or -N(R)-; t is 0, 1, 2 or 3; R, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, heterocycloalkylalkyl, alkenyl or alkynyl; R3, R4 = H, alkyl; R5 = H, alkyl, cycloalkyl, aryl, heteroaryl; R14 = H, alkyl, alkenyl, alkynyl, halo, -CN, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heterocycloalkyl, arylalkyl, heteroarylalkyl, heterocycloalkylalkyl, -OR35, N(R24)(R25) or SR35; R41 is alkyl, cycloalkyl, -S02(alkyl), -C(O)-alkyl, -C(O)-cycloalkyl or -alkyl-NH-C(O)CH3; W = (CR10R11)l; V = (CR12R13)n; Y1 = (Y)m; Y = CR30R31; l = 0 - 3; m = 0, 1; n = 0 - 3 (whereby the sum of l + n = 0 - 3); etc.] or a pharmaceutically acceptable salt or solvate thereof. Also disclosed are pharmaceutical compns. comprising the compds. I and methods of treating cognitive or neurodegenerative diseases with compds. I (no data). Also disclosed are pharmaceutical compns. and methods of treatment comprising compds. I in combination with other agents useful in treating cognitive or neurodegenerative diseases (no data).

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:722916 HCAPLUS  
DOCUMENT NUMBER: 141:207066  
TITLE: Preparation of 1-(arylsulfonyl)piperidines as  
γ-secretase inhibitors for treatment of  
neurodegenerative diseases  
INVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith,  
Elizabeth M.; Clader, John W.; Asberom, Theodros;  
Guo, Tao; Hobbs, Douglas W.  
PATENT ASSIGNEE(S): Schering-Plough Corporation, USA;  
Pharmacopeia, Inc.  
SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S.  
Ser. No. 358,898.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004171614	A1	20040902	US 2003-663042	20030916
US 2004048848	A1	20040311	US 2003-358898	20030205
WO 2005028440	A1	20050331	WO 2004-US30191	20040915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005085506	A1	20050421	US 2004-941440	20040915
PRIORITY APPLN. INFO.:			US 2002-355618P	P 20020206
			US 2003-358898	A2 20030205
			US 2003-663042	A 20030916
OTHER SOURCE(S):		MARPAT 141:207066		
GI				



AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un)substituted (hetero)aryl; R3, R3a, and R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as  $\gamma$ -secretase inhibitors, which inhibit the deposition of  $\beta$ -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K<sub>2</sub>CO<sub>3</sub>. The aldehyde was converted to the alc. with NaBH<sub>4</sub> and protected with t-BuPh<sub>2</sub>SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchloroformate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited  $\gamma$ -secretase activity in transfected human APP cells with an IC<sub>50</sub> value in the range of about 0.0002  $\mu$ M to about 15  $\mu$ M. Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

L43 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:633663 HCAPLUS

DOCUMENT NUMBER: 139:179979

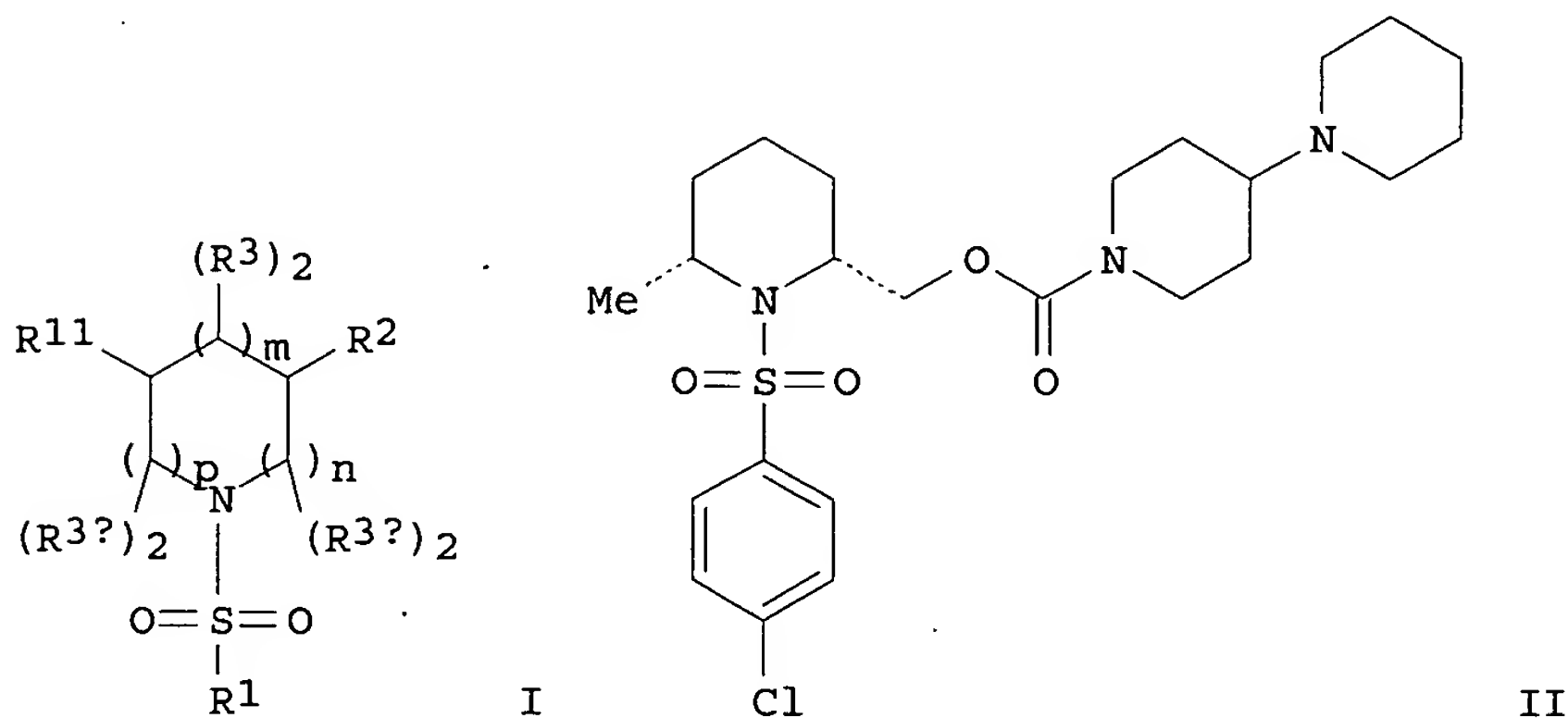
TITLE: Preparation of 1-(arylsulfonyl)piperidines as  $\gamma$ -secretase inhibitors for treatment of neurodegenerative diseases

INVENTOR(S): Pissarnitski, Dmitri A.; Josien, Hubert B.; Smith, Elizabeth M.; Clader, John W.; Asberom, Theodros; Guo, Tao; Hobbs, Douglas W.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacoepia, Inc.

SOURCE: PCT Int. Appl., 170 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003066592	A1	20030814	WO 2003-US3471	20030205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2478423	AA	20030814	CA 2003-2478423	20030205
EP 1472223	A1	20041103	EP 2003-737650	20030205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007492	A	20041123	BR 2003-7492	20030205
PRIORITY APPLN. INFO.:			US 2002-355618P	P 20020206
			WO 2003-US3471	W 20030205
OTHER SOURCE(S):		MARPAT 139:179979		
GI				



AB Title compds. I [wherein R1 = (un)substituted (hetero)aryl; R2 = alkyl, XCOY, alkylene-XCOY, alkylene-cycloalkylene-alkylene-XCOY, or (un)substitute (hetero)aryl; R3, R3a, and R3b = independently H or alkyl; R11 = (un)substituted (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; X = O, NH, N-alkyl, or O-alkylene; Y = (un)substituted amino, hydrazino, (hetero)aryl, alkyl, (hetero)cycloalkyl, etc.; m = 0-3; n = 0-3; p = 0-3; and pharmaceutically acceptable salts and solvates thereof] were prepared as  $\gamma$ -secretase inhibitors, which inhibit the deposition of  $\beta$ -amyloid protein. For example, trans-(tert-butoxycarbonyl)-2-formyl-6-methylpiperidine was epimerized using K<sub>2</sub>CO<sub>3</sub>. The aldehyde was converted



to the alc. with NaBH<sub>4</sub> and protected with t-BuPh<sub>2</sub>SiCl. Addition of 4-chlorobenzenesulfonyl chloride gave the sulfonamide. Deprotection of the alc., followed by coupling with 4-nitrophenylchloroformate, and addition of 4-(1-piperidino)piperidine provided II. The latter inhibited  $\gamma$ -secretase activity in transfected human APP cells with an IC<sub>50</sub> value in the range of about 0.0002  $\mu$ M to about 15  $\mu$ M. Thus, I and their pharmaceutical compns. are useful for the treatment of neurodegenerative disease, such as Alzheimer's disease (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:331328 HCAPLUS

DOCUMENT NUMBER: 134:326766

TITLE: Preparation of amino acid derivatives of aminobenzoic and aminobiphenylcarboxylic acids as anti-cancer agents

INVENTOR(S): Blood, Christine H.; Neustadt, Bernard R.; Smith, Elizabeth M.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S., 29 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6228985	B1	20010508	US 1998-82787	19980521
PRIORITY APPLN. INFO.:			US 1998-82787	19980521

OTHER SOURCE(S): MARPAT 134:326766

AB Compds. Q-NH(CH<sub>2</sub>)<sub>n</sub>C<sub>6</sub>H<sub>4</sub>C<sub>6</sub>H<sub>4</sub>CO-R or Q-NH(CH<sub>2</sub>)<sub>n</sub>C<sub>6</sub>H<sub>4</sub>CO-R [n is 0 or 1; R is NH<sub>2</sub> or NHCHR<sub>1</sub>R<sub>2</sub>, where R<sub>1</sub>, R<sub>2</sub> = H, alkyl, aralkyl, heteroaralkyl, carboxy, carboxyalkyl, carbamoyl; Q is R<sub>3</sub>C(O) or R<sub>4</sub>CONHCHR<sub>5</sub>CO, where R<sub>5</sub> = H, alkyl, aralkyl, heteroaralkyl, carbamoylalkyl; R<sub>3</sub>, R<sub>4</sub> = H, alkyl, alkoxy, arylalkoxy, aralkyl, heteroaralkyl, carbamoylalkyl (substituents in the biphenylcarboxylic and benzoic acids may not be in ortho,ortho'- and ortho-positions, resp.)] or biolabile esters or pharmaceutically acceptable salts were prepared. The compds. are useful for treating urokinase-type plasminogen activator (uPA) or urokinase-type plasminogen activator receptor (uPAR)-mediated disorders, e.g., tumor metastasis, tumor angiogenesis, restenosis, chronic inflammation, or corneal angiogenesis. Thus, N-[4-[4-[(3-indolylacetyl)amino]phenyl]benzoyl]-L-phenylalanine was prepared by the solid-phase method and showed IC<sub>50</sub> = 20 nM for binding of radioligand c-[<sup>125</sup>I-Tyr<sub>24</sub>]-ATFp.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:227347 HCAPLUS

DOCUMENT NUMBER: 135:55618

TITLE: Inhibition of angiogenesis and tumor growth by SCH221153, a dual  $\alpha$ v $\beta$ 3 and  $\alpha$ v $\beta$ 5 integrin receptor antagonist

AUTHOR(S): Kumar, C. Chandra; Malkowski, Michael; Yin, Zizhang; Tanghetti, Elena; Yaremko, Bo; Nechuta, Terry; Varner, Judy; Liu, Ming; Smith, Elizabeth M.; Neustadt, Bernie; Presta, Marco; Armstrong, Lydia

CORPORATE SOURCE: Department of Tumor Biology, Schering-Plough

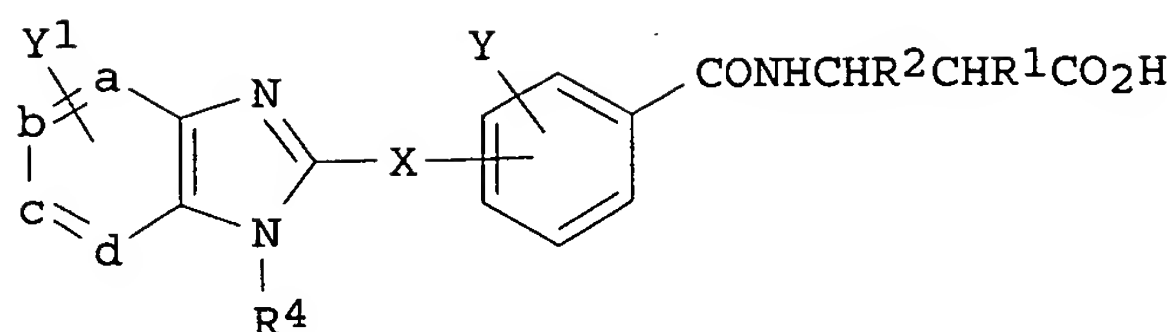


SOURCE: Research Institute, Kenilworth, NJ, 07033, USA  
Cancer Research (2001), 61(5), 2232-2238  
CODEN: CNREA8; ISSN: 0008-5472  
PUBLISHER: American Association for Cancer Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB New blood vessel formation is essential for tumor growth and metastatic spread. Integrins  $\alpha v\beta 3$  and  $\alpha v\beta 5$  are arginine-glycine-aspartic acid-dependent adhesion receptors that play a critical role in angiogenesis. Hence, selective dual  $\alpha v\beta 3$  and  $\alpha v\beta 5$  antagonists may represent a novel class of angiogenesis and tumor-growth inhibitors. Here, an arginine-glycine-aspartic acid-based peptidomimetic library was screened to identify  $\alpha v\beta 3$  antagonists. Selected compds. were then modified to generate potent and selective dual inhibitors of  $\alpha v\beta 3$  and  $\alpha v\beta 5$  receptors. One of these compds., SCH 221153, inhibited the binding of echistatin to  $\alpha v\beta 3$  ( $IC_{50} = 3.2$  nM) and  $\alpha v\beta 5$  ( $IC_{50} = 1.7$  nM) with similar potency. Its  $IC_{50}$  values for related  $\alpha 11\beta 3$  and  $\alpha 5\beta 1$  receptors were 1294 nM and 421 nM, resp., indicating that SCH 221153 is highly selective for  $\alpha v\beta 3$  and  $\alpha v\beta 5$  receptors. In cell-based assays, SCH 221153 inhibited the binding of echistatin to  $\alpha v\beta 3$ - and  $\alpha v\beta 5$ -expressing 293 cells and blocked the adhesion of endothelial cells to immobilized vitronectin and fibroblast growth factor 2 (FGF2). SCH 221153, but not the inactive analog SCH 216687, was effective in inhibiting FGF2 and vascular endothelial growth factor-induced endothelial cell proliferation in vitro with an  $IC_{50}$  equal to 3-10  $\mu$ M. Angiogenesis induced by FGF2 in the chick chorioallantoic membrane assay was also inhibited by SCH 221153. Finally, SCH 221153 exerted a significant inhibition on tumor growth induced by intradermal or s.c. injection of human melanoma LOX cells in severe combined immunodeficient mice.  
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2001:195204 HCAPLUS  
DOCUMENT NUMBER: 134:237826  
TITLE: Preparation of benzimidazole amino acid derivatives as vitronectin receptor antagonists  
INVENTOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.  
PATENT ASSIGNEE(S): Schering Corporation, USA  
SOURCE: U.S., 49 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6204282	B1	20010320	US 1999-450235	19991129
PRIORITY APPLN. INFO.:			US 1998-110302P	P 19981130
OTHER SOURCE(S):	MARPAT	134:237826		

GI



I

AB Benzimidazole amino acid derivs. I [X = (CR5R6)n(CR7R8)pNR3(CR9R10)q(CR11R12)r, which is attached at the meta or para position of the benzene ring; n, p, q, r = 0, 1; a, b, c, d represent carbon or nitrogen atom, with the proviso that no more than two of a, b, c, and d are nitrogen atoms; Y, Y' represent 1-4 optional substituents selected from alkyl, alkoxy, halo, CF3, and CO2H; R1 = H or (un)substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl, NHRA, NHCORA, NHSO2RA, NHCONHRA, or NHCO2RA (RA = H, alkyl, aryl, aralkyl, etc.); R2 = H or (un)substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl; R3 = heterocycloalkylalkyl, heterocyclocycloalkyl, CORD, SO2RE, CONRFRG, CONRFSO2RE, C(:S)NRFRG (RD, RE, RF and RG = H, alkyl, aryl, aralkyl, etc.); R5-R12 = H, alkyl] or their biolabile esters or pharmaceutically acceptable salts were prepared as vitronectin receptor antagonists. Thus, N3-[4-[[[(benzimidazol-2-ylmethyl)amino]methyl]benzoyl]-N2-(benzyloxycarbonyl)diaminopropionic acid, prepared by the solid phase method, showed IC50 = 5.4 nM for binding to the vitronectin  $\alpha v \beta 3$  receptor.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:384160 HCAPLUS

DOCUMENT NUMBER: 133:30958

TITLE: Preparation of benzimidazole amino acid derivatives as vitronectin receptor antagonists

INVENTOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

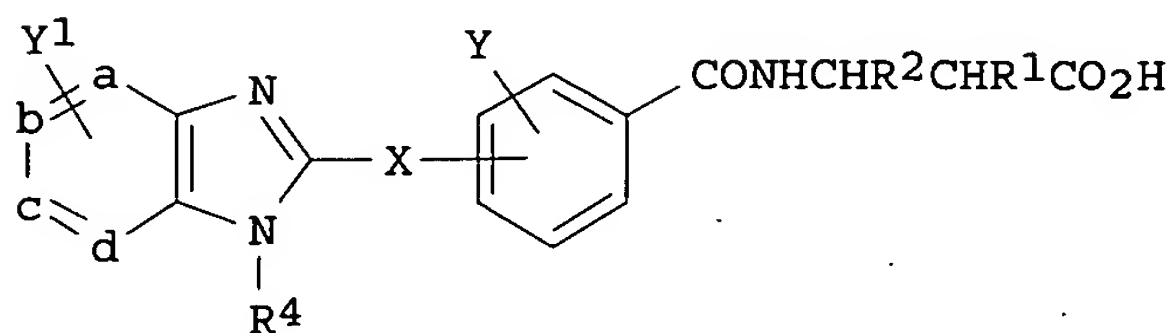
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032578	A1	20000608	WO 1999-US26023	19990929
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2353063	AA	20000608	CA 1999-2353063	19990929
EP 1135374	A1	20010926	EP 1999-962691	19990929

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO

JP 2002531441 T2 20020924 JP 2000-585220 19991129  
PRIORITY APPLN. INFO.: US 1998-201611 A 19981130  
WO 1999-US26023 W 19990929

OTHER SOURCE(S): MARPAT 133:30958  
GI



AB Benzimidazole amino acid derivs. I [X = (CR5R6)<sub>n</sub>(CR7R8)<sub>p</sub>NR3(CR9R10)<sub>q</sub>(CR11R12)<sub>r</sub>, which is attached at the meta or para position of the benzene ring; n, p, q, r = 0, 1; a, b, c, d represent carbon or nitrogen atom, with the proviso that no more than two of a, b, c, and d are nitrogen atoms; Y, Y' represent 1-4 optional substituents selected from alkyl, alkoxy, halo, CF<sub>3</sub>, and CO<sub>2</sub>H; R<sub>1</sub> = H or (un)substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl, NHRA, NHCORA, NHSO<sub>2</sub>RA, NHCONHRA, or NHCO<sub>2</sub>RA (RA = H, alkyl, aryl, aralkyl, etc.); R<sub>2</sub> = H or (un)substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl; R<sub>3</sub> = H or (un)substituted alkyl, aryl, aralkyl, arylcycloalkyl, heteroaryl, cycloalkyl, heterocycloalkyl, heteroaralkyl, cycloalkylalkyl, heterocycloalkylalkyl, CORD, CO<sub>2</sub>RD, SO<sub>2</sub>RE, CONRFGG, CONRFSO<sub>2</sub>RE, C(:S)NRFRG (RD, RE, RF and RG = H, alkyl, aryl, aralkyl, etc.); R<sub>5</sub>-12 = H, alkyl] or their biolabile esters or pharmaceutically acceptable salts were prepared as vitronectin receptor antagonists. Thus, N<sup>3</sup>-[4-[[[(benzimidazol-2-ylmethyl)amino]methyl]benzoyl]-N<sup>2</sup>-(benzyloxycarbonyl)-L-2,3-diaminopropionic acid, prepared by the solid phase method, showed IC<sub>50</sub> = 5.4 nM for binding to the vitronectin αvβ<sub>3</sub> receptor.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:630469 HCAPLUS

DOCUMENT NUMBER: 129:331038

TITLE: Construction of a family of biphenyl combinatorial libraries: structure-activity studies utilizing libraries of mixtures

AUTHOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.; Lindo, Neil; Nechuta, Terry; Bronnenkant, Alan; Wu, Arthur; Armstrong, Lydia; Kumar, Chandra

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(17), 2395-2398

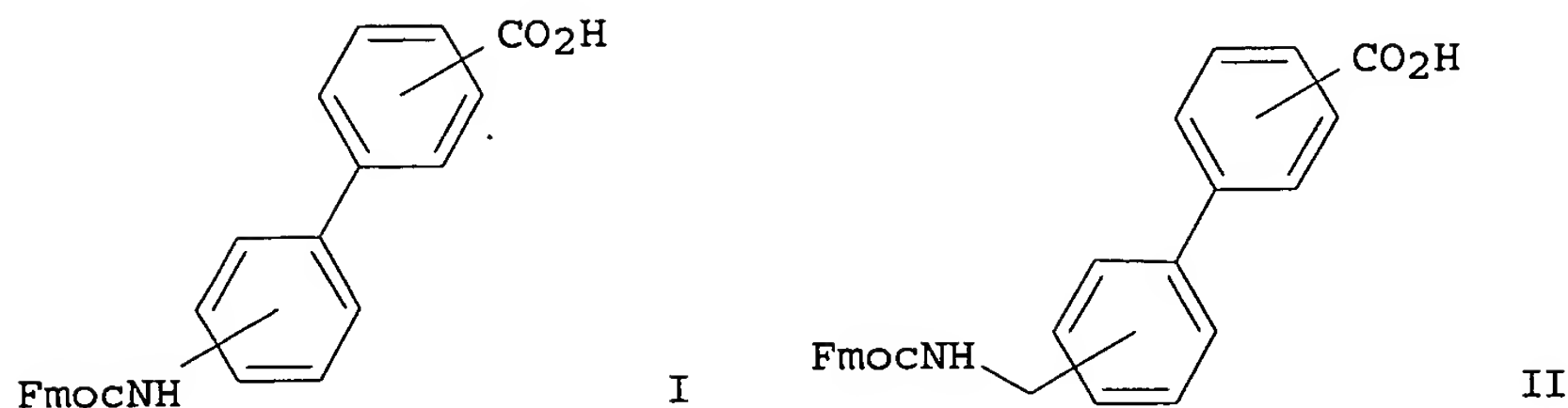
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

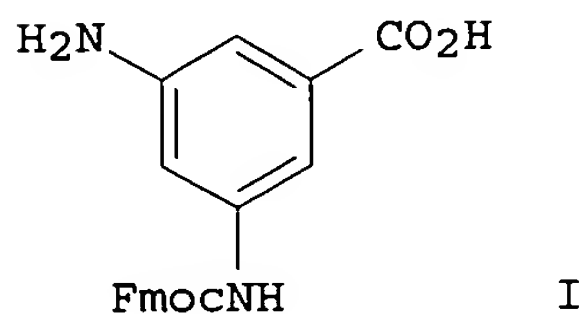
GI



AB A set of biphenyl amino acid building blocks I and II (Fmoc = 9-fluorenylmethoxycarbonyl) has been synthesized. These were used to construct partially-peptidic combinatorial libraries as equimolar multi-component samples. Activity of members of this library as vitronectin receptor antagonists is described, together with SAR studies of the most active members. These studies illustrate several important features of combinatorial libraries.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1998:454023 HCAPLUS  
 DOCUMENT NUMBER: 129:203251  
 TITLE: Combinatorial libraries based on a novel and readily accessible "centroid" scaffold  
 AUTHOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.; Nechuta, Terry; Zhang, Yongzheng  
 CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA  
 SOURCE: Tetrahedron Letters (1998), 39(30), 5317-5320  
 CODEN: TELEAY; ISSN: 0040-4039  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 129:203251  
 GI



AB A convenient large-scale preparation of the trifunctional acid I (Fmoc = 9-fluorenylmethoxycarbonyl) has been developed. This acid serves as a useful scaffold for construction of combinatorial libraries incorporating three variable elements in a centro-sym. array.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1997:436013 HCAPLUS  
 DOCUMENT NUMBER: 127:95514

TITLE: Potent Tetracyclic Guanine Inhibitors of PDE1 and PDE5  
Cyclic Guanosine Monophosphate Phosphodiesterases with  
Oral Antihypertensive Activity

AUTHOR(S): Ahn, Ho-Sam; Bercovici, Ana; Boykow, George;  
Bronnenkant, Alan; Chackalamannil, Samuel; Chow,  
Jason; Cleven, Renee; Cook, John; Czarniecki, Michael;  
Domalski, Carol; Fawzi, Ahmad; Green, Michael;  
Guendes, Asli; Ho, Ginny; Laudicina, Malvina; Lindo,  
Neil; Ma, Ke; Manna, Mahua; McKittrick, Brian; Mirzai,  
Bitu; Nechuta, Terry; Neustadt, Bernard; Puchalski,  
Chester; Pula, Kathryn; Silverman, Lisa; **Smith,  
Elizabeth**; Stamford, Andrew; Tedesco, Richard P.;  
Tsai, Hsinging; Tulshian, Deen; Vaccaro, Henry;  
Watkins, Robert W.; Weng, Xiaoyu; Witkowski, Joseph  
T.; Xia, Yan; Zhang, Hongtao

CORPORATE SOURCE: **Schering-Plough Research Institute, Kenilworth,  
NJ, 07033, USA**

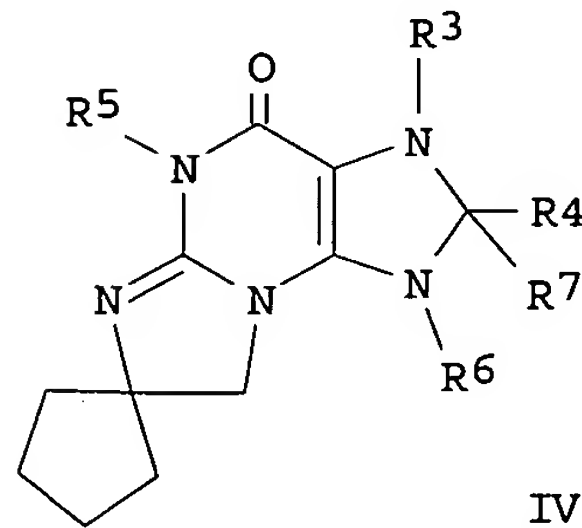
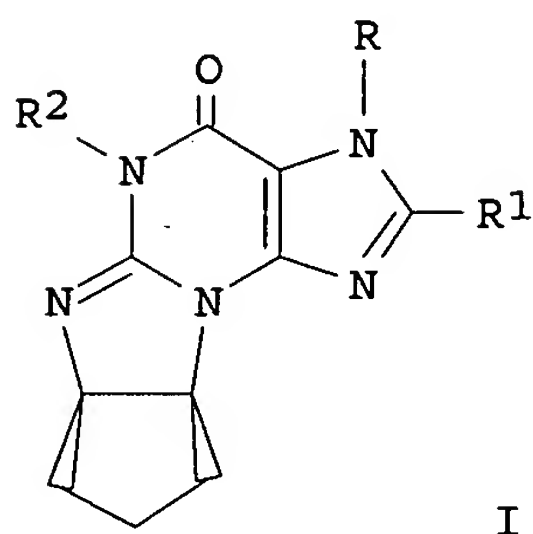
SOURCE: Journal of Medicinal Chemistry (1997), 40(14),  
2196-2210  
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

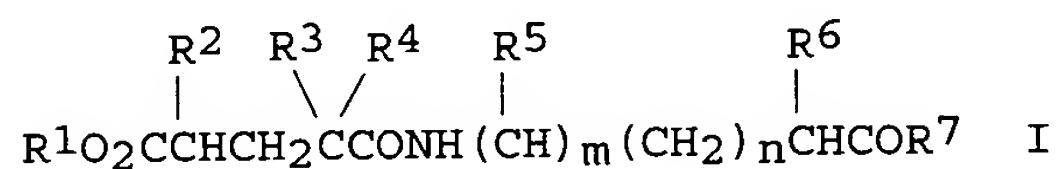


AB Tetracyclic guanines I, IV have been shown to be potent and selective inhibitors of the cGMP-hydrolyzing enzymes PDE1 and PDE5. In general, these compds. are inactive or only weakly active as inhibitors of PDE3, which is a major isoenzyme involved in cAMP hydrolysis. Structure-activity relationships are developed at N-1, C-2, N-3, and N-5 on the core nucleus. Compound I [R = CH<sub>2</sub>Ph; R<sub>1</sub> = CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>Ph-4; R<sub>2</sub> = Me (II)], with an IC<sub>50</sub> of 70 pM, is the most potent inhibitor of PDE1, while I [R = CH<sub>2</sub>Ph; R<sub>1</sub> = C.tplbond.CPh; R<sub>2</sub> = Me (III)], with an IC<sub>50</sub> of 4 nM, is the most potent inhibitor of PDE5. Compds. e.g. IV [R<sub>3</sub> = H; R<sub>4</sub> = cyclopentylmethyl; R<sub>5</sub> = Me; R<sub>6</sub>, R<sub>7</sub> = bond (V)] and III are potent dual inhibitors with IC<sub>50</sub> values below 30 nM for both PDE1 and PDE5. Compds. I (R = H; R<sub>1</sub> = hexyl; R<sub>2</sub> = Me; R = H: R<sub>1</sub> = CH<sub>2</sub>Ph; R<sub>2</sub> = Me) and V reduced blood pressure by more than 45 mm Hg when administered orally at 10 mg/kg to the spontaneously hypertensive rat (SHR).

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1995:420794 HCAPLUS  
 DOCUMENT NUMBER: 123:228893  
 TITLE: Carboxyalkylcarbonyl amino acid endopeptidase inhibitors  
 INVENTOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.; Haslanger, Martin F.  
 PATENT ASSIGNEE(S): Schering Corp., USA  
 SOURCE: U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 439,765. CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 5389610	A	19950214	US 1992-849036	19920421
WO 9107386	A1	19910530	WO 1990-US6655	19901120
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1989-439765	A2 19891121
			WO 1990-US6655	W 19901120
OTHER SOURCE(S):		MARPAT 123:228893		
GI				



AB Carboxyalkylcarbonyl amino acid inhibitors of endopeptidases of the formula I or pharmaceutically acceptable salt thereof, wherein R<sup>1</sup> is H, alkyl, arylalkyl, aryl or aryloxyalkyl; R<sup>2</sup> is alkyl, alkenyl, alkynyl, alkoxy or alkylthio, wherein the alkyl portion is substituted with 0-3 substituents independently selected from the group consisting of hydroxy, alkoxy, alkoxyalkoxy, alkylthio, aryl, alkoxyalkylthio, arylalkoxy and arylalkylthio; R<sup>3</sup> and R<sup>4</sup> are independently alkyl or arylalkyl; or R<sup>3</sup> and R<sup>4</sup> together with the carbon to which they are attached form an optionally substituted 5-, 6- or 7-membered ring wherein said ring comprises 0 to 1 heteroatoms selected from the group consisting of sulfur and oxygen; R<sup>5</sup> is H, alkyl, alkoxyalkyl, alkylthioalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, arylalkoxyalkyl or arylalkylthioalkyl; R<sup>6</sup> is H, hydroxy, alkoxy, alkyl, arylalkoxy, alkoxyalkyl, alkylthioalkyl, arylalkoxyalkyl, arylalkylthioalkyl, aryl or heteroaryl; R<sup>7</sup> is hydroxy, alkoxy, aryloxy, arylalkoxy, amino, alkylamino or dialkylamino; m is 0 or 1; and n is 0, 1, 2 or 3, use of the compds., alone or in combination with an ACE inhibitor or an ANF, in the treatment of cardiovascular disorders such as hypertension, congestive heart failure, edema and renal insufficiency, use of the compds. in the treatment of nephrotoxicity and pain conditions (no data), and pharmaceutical compns. containing said compds. are disclosed. Pharmaceutical formulations were given. Thus, e.g., N-[1-[2(R,S)-carboxy-4-phenylbutyl]cyclopentanecarbonyl]-(L)-methionine was prepared by a consecutive series of reactions involving addition of cyclopentanecarboxylic acid with t-Bu 2-(2-phenylethyl)acrylate to afford 1-(2-t-Butoxycarbonyl-4-



phenylbutyl)cyclopentanecarboxylic acid, followed by coupling with (S)-methionine Et ester hydrochloride.

L43 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:264514 HCAPLUS

DOCUMENT NUMBER: 122:56581

TITLE: Preparation of peptide analogs as inhibitors of neutral endopeptidase and angiotensin converting enzyme.

INVENTOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.; Tulshian, Deen

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 95 pp.

CODEN: PIXXD2

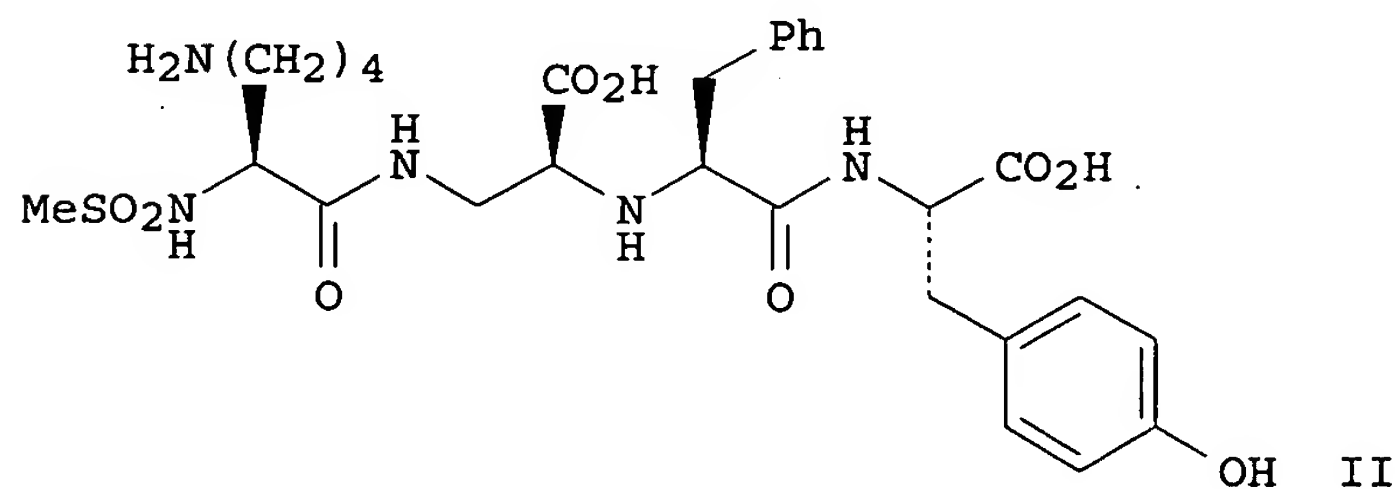
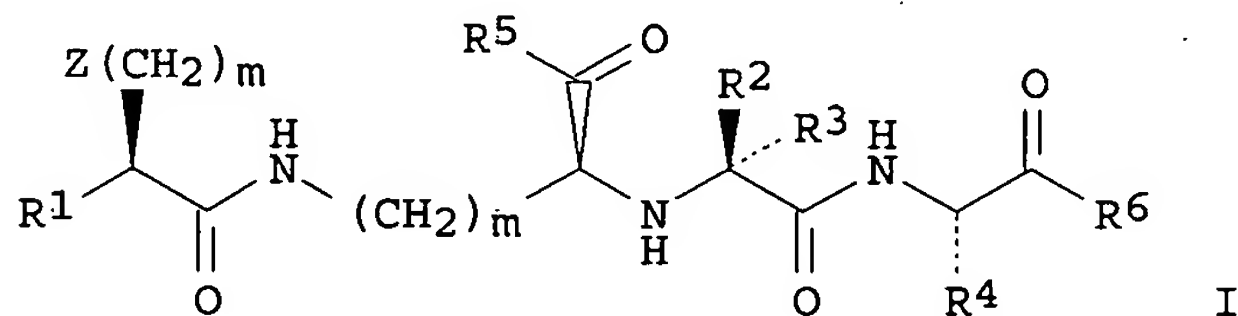
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9403481	A1	19940217	WO 1993-US7137	19930803
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5298492	A	19940329	US 1992-925338	19920804
AU 9347919	A1	19940303	AU 1993-47919	19930803
EP 658169	A1	19950621	EP 1993-918488	19930803
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07509717	T2	19951026	JP 1993-505432	19930803
PRIORITY APPLN. INFO.:			US 1992-925338	A2 19920804
			WO 1993-US7137	W 19930803
OTHER SOURCE(S):		MARPAT 122:56581		
GI				



AB Title compds. [I; Z = amino, alkylamino, dialkylamino, R9CONH, (substituted) guanidino; R1 = H, R7R8N; R2 = H, alkyl, cycloalkyl, arylalkyl, heteroarylalkyl; R3 = H, alkyl or cycloalkyl; R2R3C = 3-7

membered carbocyclic ring; R4 = H, alkyl, arylalkyl or heteroarylalkyl; R5, R6 = OH, alkoxy, amino, arylalkoxy, alkylamino, dialkylamino; R7 = R9CO, R10SO2; R8 = H, alkyl, arylalkyl, aryl; R7R8N = 5-7 membered ring; R9 = alkyl, arylalkyl, aryl, heteroarylalkyl, heteroaryl, alkoxy, arylalkoxy, amino, alkylamino, dialkylamino; R10 = alkyl, arylalkyl, aryl, heteroarylalkyl, amino, alkylamino, dialkylamino, heteroaryl; m, n = 1-5], were prepared Thus, title compound II (solution phase preparation given) inhibited ACE with IC50 = 50 nM.

L43 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:499078 HCAPLUS  
DOCUMENT NUMBER: 121:99078  
TITLE: Mercaptoacyl amino acid inhibitors of atriopeptidase.  
1. Structure-activity relationship studies of methionine and S-alkylcysteine derivatives  
AUTHOR(S): Neustadt, Bernard R.; **Smith, Elizabeth M.**; Nechuta, Terry L.; Bronnenkant, Alan A.; Haslanger, Martin F.; Watkins, Robert W.; Foster, Caroline J.; Sybertz, Edmund J.  
CORPORATE SOURCE: **Schering-Plough Research Institute, Kenilworth, NJ, 07033-0539, USA**  
SOURCE: Journal of Medicinal Chemistry (1994), 37(15), 2461-76  
CODEN: JMCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A broad series of N-(3-mercaptoacyl) amino acid derivs. was evaluated for their ability to inhibit atriopeptidase (neutral endopeptidase, EC 3.4.24.11) in vitro and in vivo. Structural parameters studied were (i) the substituent on the 2-position of the 3-mercaptopropionyl moiety, (ii) the amino acid component, (iii) the S-terminal derivative, and (i.v.) the C-terminal derivative Optimum activity was observed for derivs. of methionine and S-alkylcysteines. N-[3-Mercapto-2(S)-[(2-methylphenyl)methyl]-1-oxopropyl]-L-methionine was identified as a highly effective inhibitor of atriopeptidase meriting evaluation as a potential cardiovascular therapeutic agent.

L43 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:236168 HCAPLUS  
DOCUMENT NUMBER: 116:236168  
TITLE: Preparation of (mercaptoacylamino)acids for treatment of hypertension and congestive heart failure.  
INVENTOR(S): Haslanger, Martin F.; Neustadt, Bernard R.; **Smith, Elizabeth M.**  
PATENT ASSIGNEE(S): **Schering Corp., USA**  
SOURCE: U.S., 22 pp. Cont.-in-part of U.S. 4,801,609.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5061710	A	19911029	US 1987-133669	19871216
US 4801609	A	19890131	US 1987-32153	19870327
EP 254032	A2	19880127	EP 1987-108730	19870617
EP 254032	A3	19900905		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 08283153	A2	19961029	JP 1995-246555	19870619



## Ward 10\_663042-inventor search

US 4929641	A	19900529	US 1988-192435	19880511
US 4929641	B1	19940830		
WO 8905796	A1	19890629	WO 1988-US4376	19881213
W: AU, BB, BG, BR, DK, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
EP 322633	A1	19890705	EP 1988-120795	19881213
EP 322633	B1	19910522		
R: ES, GR				
AU 8928002	A1	19890719	AU 1989-28002	19881213
AU 615976	B2	19911017		
EP 390839	A1	19901010	EP 1989-900561	19881213
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02503799	T2	19901108	JP 1989-500640	19881213
HU 54979	A2	19910429	HU 1989-380	19881213
HU 204781	B	19920228		
AT 63741	E	19910615	AT 1988-120795	19881213
ES 2039578	T3	19931001	ES 1988-120795	19881213
CN 1033803	A	19890712	CN 1988-108633	19881214
ZA 8809373	A	19900829	ZA 1988-9373	19881214
DK 9001468	A	19900615	DK 1990-1468	19900615
NO 9002687	A	19900615	NO 1990-2687	19900615
US 4801609	B1	19931109	US 1991-90002282	19910214
US 5262436	A	19931116	US 1991-741025	19910806
PRIORITY APPLN. INFO.:			US 1987-32153	A2 19870327
			EP 1987-108730	A 19870617
			US 1986-876610	A 19860620
			JP 1987-153219	A3 19870619
			US 1987-133669	A2 19871216
			EP 1988-120795	A 19881213
			WO 1988-US4376	A 19881213

## OTHER SOURCE(S):

MARPAT 116:236168

AB Q-CH<sub>2</sub>CH[(CH<sub>2</sub>)<sub>n</sub>R<sub>1</sub>]CONHCHR<sub>2</sub>COR<sub>3</sub> [R<sub>1</sub> = YC<sub>6</sub>H<sub>4</sub>XC<sub>6</sub>H<sub>4</sub>; YC<sub>6</sub>H<sub>4</sub>, YC<sub>6</sub>H<sub>4</sub>S, etc.; R<sub>2</sub> = alkyl, (alkylsulfonyl)alkyl, (alkylsulfinyl)alkyl, etc.; R<sub>3</sub> = (substituted) hydroxy, (substituted) amino, etc.; Q = H, alkanoyl, etc.; n = 0-2; X = bond, O, S, CH<sub>2</sub>; Y = H, alkyl, cycloalkyl, alkoxy, OH, F, etc.]and their pharmaceutically acceptable salts, useful for treatment of hypertension and congestive heart failure (no data), are prepared

S-(4-Methylbenzyl)-L-cysteine Me ester hydrochloride (preparation given) was acylated with 3-(acetylthio)-2-benzylpropionic acid and the resulting diastereomeric mixture of N-[3-(acetylthio)-2-benzylpropionyl]-S-(4-methylbenzyl)-L-cysteine Me ester was treated with MeOH-1N NaOH at 0 to -5° for 6 h to give the corresponding diastereomeric mixture of N-(2-benzyl-3-mercaptopropionyl)-S-(4-methylbenzyl)-L-cysteine.

L43 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:174770 HCAPLUS

DOCUMENT NUMBER: 116:174770

TITLE: Preparation of disulfide derivatives of mercaptoacylamino acids as cardiovascular agents

INVENTOR(S): Haslanger, Martin F.; Neustadt, Bernard R.;

Smith, Elizabeth M.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9117980	A1	19911128	WO 1991-US3251	19910515
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9179572	A1	19911210	AU 1991-79572	19910515
ZA 9103685	A	19920226	ZA 1991-3685	19910515
EP 528997	A1	19930303	EP 1991-911546	19910515
EP 528997	B1	19950201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05502038	T2	19930415	JP 1991-510190	19910515
JP 06102648	B4	19941214		
ES 2069893	T3	19950516	ES 1991-911546	19910515
PRIORITY APPLN. INFO.:			US 1990-525370	A2 19900517
			WO 1991-US3251	A 19910515

OTHER SOURCE(S): MARPAT 116:174770

AB [SCH2CH(CH2R1)nCONHCHR2CHR4(CH2)t(CHR9)pCOR3]2,  
[SCH2CH(CH2R7)nCONHCHR2COR3 [R1 = alkyl, cycloalkyl, aryl, heteroaryl; R2 = H, alkyl, cycloalkyl, hydroxyalkyl, alkoxy, HS, alkylthio, aryl, heteroaryl, aralkyloxy, aralkylthio, R3 = R5O, R5R6N, R5, R6 = H, alkyl, hydroxyalkyl, etc., R5R6N = 5-7-membered ring; R4, R9 = (CH2)qR8, R8 = H, HO, alkoxy, HS, alkylthio, aryl, heteroaryl; R7 = (substituted) Ph; n = 1, 2; p, t = 0, 1; q = 0-2] useful in treatment of cardiovascular disorders and pain, are prepared To N-[3-mercapto-2(S)-(2-methylbenzyl)propionyl]-(S)-methionine Et ester (preparation given) in absolute EtOH was added iodine/EtOH to

give 1,1'-[dithiobis[2(S)-(2-methylbenzyl)-1-oxo-3,1-propanediyl]]bis-(S)-methionine di-Et ester, which produced a drop in pressure in the DOCA salt model in the atrial natriuretic factor potentiation procedure.  
Pharmaceutical formulations containing the title compds. are given.

L43 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:632870 HCAPLUS

DOCUMENT NUMBER: 115:232870

TITLE: Preparation of carboxyalkylcarbonyl amino acid endopeptidase inhibitors

INVENTOR(S): Neustadt, Bernard R.; Smith, Elizabeth M.; Haslanger, Martin F.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9107386	A1	19910530	WO 1990-US6655	19901120
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2069112	AA	19910522	CA 1990-2069112	19901120
AU 9168802	A1	19910613	AU 1991-68802	19901120
EP 502075	A1	19920909	EP 1991-900076	19901120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				

## Ward 10\_663042-inventor search

JP 05501111	T2	19930304	JP 1991-500851	19901120
JP 07005530	B4	19950125	JP 1990-500851	19901120
US 5389610	A	19950214	US 1992-849036	19920421
PRIORITY APPLN. INFO.:			US 1989-439765	A2 19891121
			WO 1990-US6655	A 19901120

OTHER SOURCE(S): MARPAT 115:232870

AB Endopeptidase-inhibiting carboxyalkylcarbonyl amino acids  
R1OCOCHR2CH2CR3R4CONH(CHR5)m(CH2)nCHR6COR7 [I; R1 = H, alkyl, aralkyl, aryloxyalkyl; R2 = (substituted) alkyl, alkenyl, alkynyl, alkoxy, alkylthio; R3, R4 = alkyl, aralkyl, or CR3R4 = (substituted or benzo-fused) 5-7 membered ring which may contain one O or S atom; R5 = alkyl, alkoxyalkyl, alkylthioalkyl, aryl, heteroaryl, etc.; R6 = OH, alkoxy, alkyl, aralkoxy, alkoxyalkyl, etc.; R7 = OH, alkoxy, aryloxy, aralkoxy, NH2, alkylamino, dialkylamino; m = 0, 1; n = 0-3], useful as cardiovascular agents (no data), analgesics (no data), and useful for the treatment of nephrotoxicity (no data), were prepared. Thus, cyclopentanecarboxylic acid was treated with 2 equiv LDA followed by Ph(CH2)2CH:CHCO2CMe3 and the product was coupled with (S)-methionine Et ester hydrochloride to give N-[1-(2-tert-butoxycarbonyl-4-phenylbutyl)-cyclopentanecarbonyl]-(S)-methionine Et ester. The esters groups were sequentially hydrolyzed by treatment with TFA then 1.0N NaOH to give racemic N-[1-(2-carboxy-4-phenylbutyl)cyclopentanecarbonyl]-(S)-methionine. Formulations of I were prepared

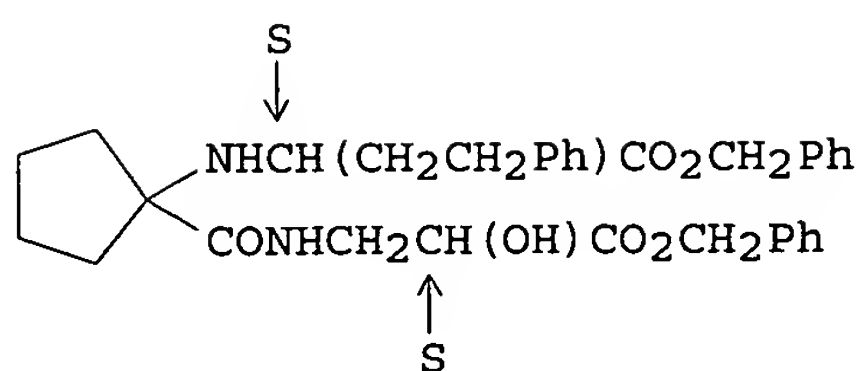
L43 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:559812 HCAPLUS  
DOCUMENT NUMBER: 115:159812  
TITLE: Preparation of endopeptidase-inhibiting carboxyalkyl dipeptides as analgesics and cardiovascular agents  
INVENTOR(S): Haslanger, Martin F.; Neustadt, Bernard R.;  
Smith, Elizabeth M.  
PATENT ASSIGNEE(S): Schering Corp., USA  
SOURCE: PCT Int. Appl., 47 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9105796	A1	19910502	WO 1990-US5640	19901010
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9065033	A1	19910516	AU 1990-65033	19901010
EP 495822	A1	19920729	EP 1990-914812	19901010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05501247	T2	19930311	JP 1990-513846	19901010
PRIORITY APPLN. INFO.:			US 1989-421041	A2 19891013
			WO 1990-US5640	A 19901010

OTHER SOURCE(S): MARPAT 115:159812

GI



AB Endopeptidase-inhibiting carboxyalkyl dipeptides  
 $R_1O_2COCHR_2NHCHR_3R_4CONH(CHR_5)_m(CH_2)_nCHR_6COR_7$  [ $R_1 = H$ , alkyl, aralkyl aryl;  $R_2 = H$ , (substituted) alkyl, alkenyl, alkynyl;  $R_3, R_4 =$  alkyl, aralkyl or  $R_3R_4 =$  (substituted) 5-7 membered ring which may contain one S or O atom;  $R_5 = H$ , alkyl, alkoxyalkyl, aryl, heteroaryl, etc.;  $R_6 = H$ , OH, alkoxy, alkyl, alkoxyalkyl, etc.;  $R_7 = OH$ , alkoxy, aryloxy, aralkoxy, (di)alkylamino;  $m = 0, 1$ ;  $n = 0-3$ ] useful as analgesics (no data) and cardiovascular agents (no data), were prepared. Thus, 2(R)-Acetoxy-4-phenylbutyric acid (preparation given) was hydrolyzed by NaOH and the resulting hydroxy acid was converted to its benzyl ester and the latter converted to the triflate. Treatment of the triflate with tert-Bu 1-aminocyclopentane-1-carboxylate (preparation given) gave 1-[1S-benzyloxycarboxy-3-phenylpropyl]aminocyclopentanecarboxylic acid as the HCl salt, which was coupled with (S)-isoserine benzyl ester. HCl to give title dipeptide I. The title dipeptides are formulated as tablets and capsules.

L43 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:186065 HCAPLUS

DOCUMENT NUMBER: 114:186065

TITLE: Preparation of N-(mercaptoacyl)amino acids as cardiovascular agents

INVENTOR(S): **Smith, Elizabeth M.**; DeCapite, Philip M.; Neustadt, Bernard R.

PATENT ASSIGNEE(S): **Schering Corp., USA**

SOURCE: Eur. Pat. Appl., 30 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 393441	A1	19901024	EP 1990-106655	19900406
EP 393441	B1	19930526		
R: GR				
ZA 9002661	A	19910130	ZA 1990-2661	19900405
CA 2051652	AA	19901011	CA 1990-2051652	19900406
WO 9012003	A1	19901018	WO 1990-US1787	19900406
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9054363	A1	19901105	AU 1990-54363	19900406
AU 633079	B2	19930121		
EP 467957	A1	19920129	EP 1990-906554	19900406
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
HU 58286	A2	19920228	HU 1990-3561	19900406
HU 209778	B	19941028		

## Ward 10\_663042-inventor search

JP 04504130	T2	19920723	JP 1990-506159	19900406
JP 07000593	B4	19950111		
AT 89817	E	19930615	AT 1990-106655	19900406
ES 2055207	T3	19940816	ES 1990-106655	19900406
US 5219886	A	19930615	US 1991-768647	19911001
NO 9103956	A	19911009	NO 1991-3956	19911009
PRIORITY APPLN. INFO.:			US 1989-335264	A 19890410
			EP 1990-106655	A 19900406
			WO 1990-US1787	A 19900406

OTHER SOURCE(S): MARPAT 114:186065

AB QSCH2CH[(CH2)nR1]CONHCHR2CHR4(CH2)t(CHR5)pCOR3 [I; Q = H, CHO, alkanoyl, aroyl; R1 = (cyclo)alkyl, (hetero)aryl; R2 = H, (cyclo)alkyl, (substituted) alkyl, (hetero)aryl; R3 = (substituted) OH or NH2; R4, R5 = (CH2)qR6; R6 = H, OH, alkoxy, SH, alkylthio, heteroaryl; q = 0, 1, 2; t = 0, 1], which also inhibit enkephalinase A and thus elicit analgesic effect (no data), and a pharmaceutical composition for treating hypertension, congestive heart failure, edema, renal insufficiency, or pain (no data) containing I alone or in combination with an atrial natriuretic factor or an angiotensin converting enzyme inhibitor are prepared. Thus, a mixture of 2(S)-acetylthiomethyl-3-(2-methylphenyl)propionic acid, (S)-isoserine Et ester-HCl (preparation given, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide-HCl, and 1-hydroxybenzotriazole in DMF was stirred 20 h to give N-[2(S)-acetylthiomethyl-3-(2-methylphenyl)propanoyl]-(S)-isoserine Et ester. Tablets containing N-[2(S)-mercaptomethyl-3-(2-methylphenyl)propanoyl]-(S)-isoserine are prepared.

L43 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:158967 HCAPLUS

DOCUMENT NUMBER: 112:158967

TITLE: Preparation of mercapto-acylamino acid antihypertensives

INVENTOR(S): Haslanger, Martin F.; Neustadt, Bernard Ray; Smith, Elizabeth Melva

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
EP 322633	A1	19890705	EP 1988-120795	19881213
EP 322633	B1	19910522		
R: ES, GR				
US 5061710	A	19911029	US 1987-133669	19871216
AT 63741	E	19910615	AT 1988-120795	19881213
PRIORITY APPLN. INFO.:			US 1987-133669	A 19871216
			US 1987-32153	A2 19870327
			EP 1987-108730	A 19870617
			EP 1988-120795	A 19881213

AB QSCH2CH[(CH2)nR1]CONHCHR2COR3 [I; R1 = YC6H4, YC6H4S, YC6H4O, naphthyl, furyl, thienyl, benzofuryl, benzothienyl, Ph2CH, etc.; R2 = R4(CH2)kSOn(CH2)q, R5O2C(CH2)q; R3 = OR7, NR7R8, NHCHR9CONR7R8, NHCHR9CO2R7, OCHR9CONR7R8; R4 = alkenyl, alkoxy, alkylthio, OH; R5 = dihydroalkyl, dialkoxyalkyl, alkoxyalkoxyalkyl, haloalkyl, etc.; R7, R8 = H, R5, alkyl, hydroxyalkyl, aminoalkyl, arylalkyl, etc.; R7R8N = (substituted) heterocyclyl; R9 = H, alkyl, carboxyalkyl, guanidinoalkyl, indolylalkyl, mercaptoalkyl, etc.; R10 = alkyl, hydroxyalkyl, alkoxyalkyl,

diaminoalkyl, naphthyl, furyl, thienyl, pyridyl, etc.; Q = H, R10CO; YY1 = H, alkyl, cycloalkyl, alkoxy, OH, F, Cl, Br, cyano, CH2NH2, CO2H, Ph, etc.; k = 1-3; m,n = 0-2; q = 1-4], useful as antihypertensives and adjuvants for atrial natriuretic factors or angiotensin converting enzyme inhibitors, were prepared Thus, a mixture of 3-benzoylthio-2(S)-benzylpropionic acid, S-allyl-(R)-cysteinamide hydrochloride, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, 1-hydroxybenzotriazole, and N-methylmorpholine was stirred 20 h in DMF to give N-[3-benzoylthio-2(S)-benzylpropionyl]-S-allyl-(R)-cysteinamide.

L43 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:595414 HCAPLUS

DOCUMENT NUMBER: 111:195414

TITLE: Preparation of N-(carboxyalkyl)dipeptides for treatment of hypertension and congestive heart failure and pharmaceutical compositions containing them

INVENTOR(S): Gold, Elijah H.; Neustadt, Bernard R.; **Smith, Elizabeth M.**PATENT ASSIGNEE(S): **Schering Corp., USA**

SOURCE: U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 29;293.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

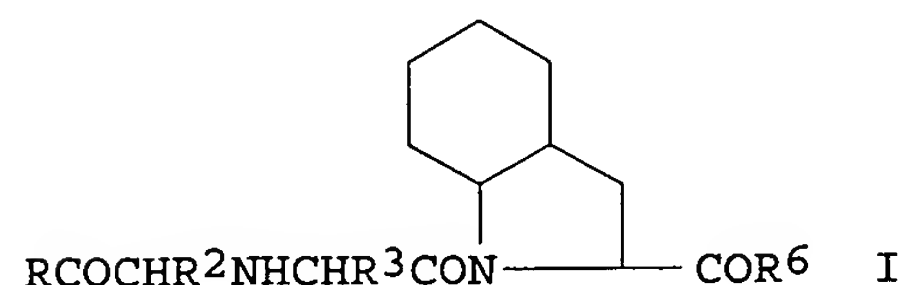
FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4818749	A	19890404	US 1987-117008	19871104
EP 50800	A1	19820505	EP 1981-108348	19811015
EP 50800	B1	19860618		
EP 50800	B2	19950607		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
ZA 8107261	A	19820929	ZA 1981-7261	19811020
US 4808573	A	19890228	US 1987-29293	19870323
PRIORITY APPLN. INFO.:			US 1980-199886	A2 19801023
			US 1980-201649	A2 19801028
			US 1981-258484	A2 19810428
			EP 1981-108348	A 19811015
			US 1981-334053	A2 19811223
			US 1987-29293	A2 19870323

OTHER SOURCE(S): MARPAT 111:195414

GI

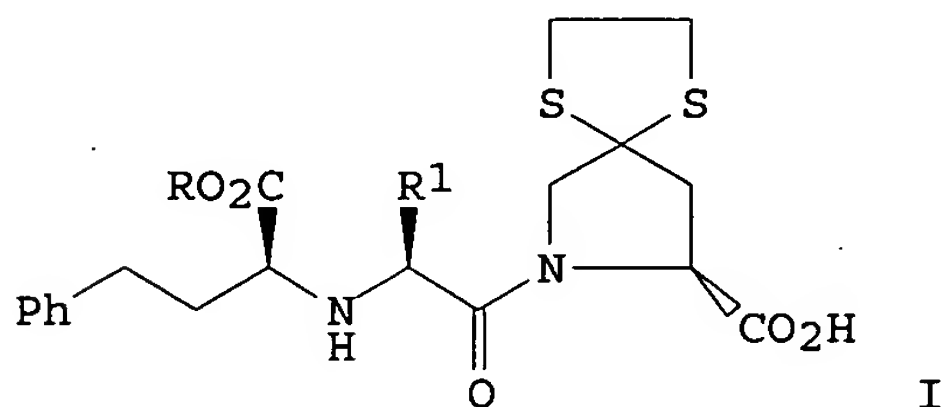


AB Angiotensin converting enzyme inhibitors I [R, R<sub>6</sub> = OH, alkoxy; R<sub>2</sub> = PhCH<sub>2</sub>S, PhCH<sub>2</sub>CH<sub>2</sub>SCH<sub>2</sub>, naphthylmethylthiomethyl, etc.; R<sub>3</sub> = H, (amino)alkyl], useful for treatment of hypertension and congestive heart failure, are prepared (S)-(4-Methylbenzyl)-L-cysteine Et ester was reacted with N-pyruvoyl-(S)-perhydroindole in THF-EtOH containing NaBH<sub>3</sub>CN to give 1-[N-[1(R)-(ethoxycarbonyl)-2-(4-methylbenzylthio)ethyl]-(R,S)-alanyl]-



cis,syn-perhydroindole-2(S)-carboxylic acid. Most of the 11 I tested as inhibitors of angiotensin converting enzyme showed activity comparable to that of captopril. A total of 13 I were prepared with data. A hard gelatin capsule was formulated containing I (unspecified) 125.0, lactose 173.0, corn starch 75.0, and Mg stearate 2.0 mg is described.

L43 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1989:554371 HCAPLUS  
 DOCUMENT NUMBER: 111:154371  
 TITLE: Angiotensin converting enzyme inhibitors: spirapril and related compounds  
 AUTHOR(S): Smith, Elizabeth M.; Swiss, Gerald F.; Neustadt, Bernard R.; McNamara, Paul; Gold, Elijah H.; Sybertz, Edmund J.; Baum, Thomas  
 CORPORATE SOURCE: Dep. Med. Chem., Schering-Plough Corp., Bloomfield, NJ, 07003, USA  
 SOURCE: Journal of Medicinal Chemistry (1989), 32(7), 1600-6  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 111:154371  
 GI

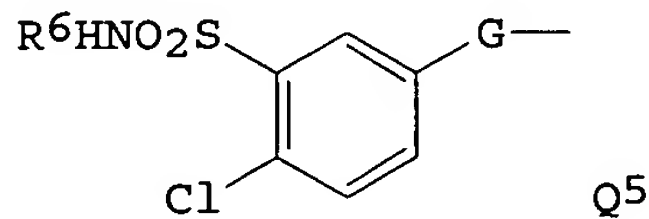
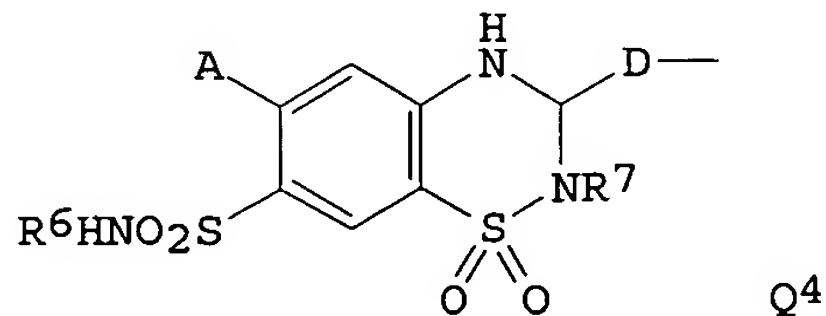
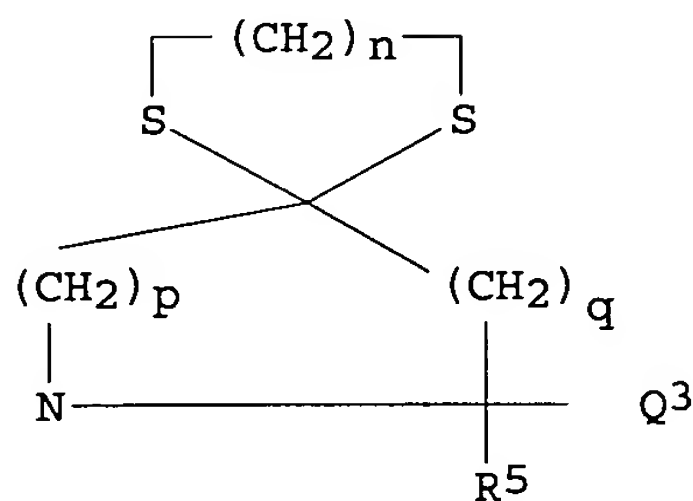
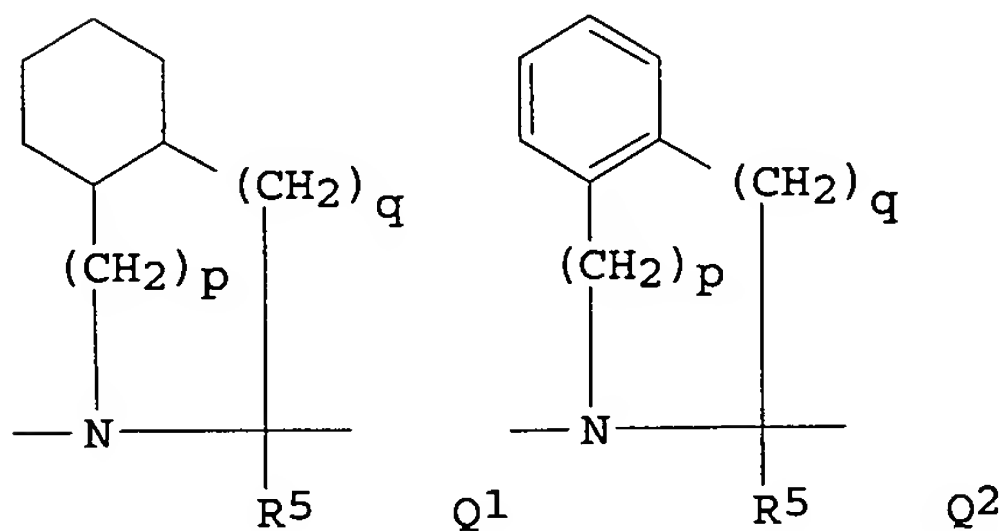
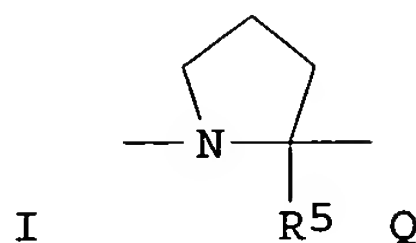
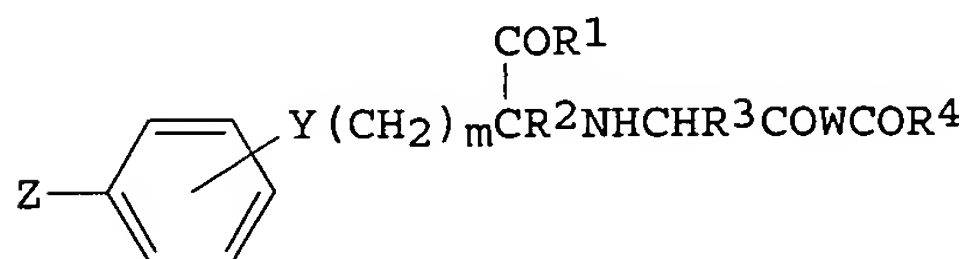


AB The synthesis of spirapril (I, R = Et, R1 = Me) (II), spiraprilat (I, R = H, R1 = Me) (III), their (RSS) stereoisomers, and their glycyl (I, R = Et, R1 = H) and lysyl [I, R = H, Et, R1 = (CH2)4NH2] analogs is described. These compds. were evaluated in vivo for inhibition of angiotensin converting enzyme (ACE), and selected compds. were evaluated for in vitro ACE inhibition (II ID50 16 µg/kg; III IC50 0.8 nM, ID50 8 µg/kg). In anesthetized rats (i.v.), esters II and I [R = Et, R1 = (CH2)4NH2] are more potent than enalapril, and diacids III and I [R = H, R1 = (CH2)4NH2] are more potent than enalaprilat in vitro. In the conscious rats (orally), II and enalapril showed potent and sustained activity at doses of 0.03-1 and 0.1-1 mg/kg, resp. From this work, II was selected for clin. evaluation as an antihypertensive agent.

L43 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1989:546828 HCAPLUS  
 DOCUMENT NUMBER: 111:146828  
 TITLE: Carboxyalkyl dipeptide derivatives as drugs for glaucoma treatment  
 INVENTOR(S): Watkins, Robert; Doll, Ronald J.; Neustadt, Bernard R.; Smith, Elizabeth M.; Magatti, Charles V.; Gold, Elijah H.  
 PATENT ASSIGNEE(S): Schering Corp., USA  
 SOURCE: U.S., 17 pp. Cont.-in-part of U.S. Ser. No. 651,378.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 4783444	A	19881108	US 1986-849072	19860404
US 4584285	A	19860422	US 1984-651378	19840917
AU 8548088	A1	19870407	AU 1985-48088	19850916
AU 581929	B2	19890309		
EP 236307	A1	19870916	EP 1985-904731	19850916
EP 236307	B1	19910417		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63500938	T2	19880407	JP 1985-504147	19850916
AT 62694	E	19910515	AT 1985-904731	19850916
FI 8702110	A	19870513	FI 1987-2110	19870513
NO 8701982	A	19870513	NO 1987-1982	19870513
US 4840772	A	19890620	US 1988-227954	19880803
PRIORITY APPLN. INFO.:			US 1983-500494	A1 19830602
			US 1984-651378	A2 19840917
			EP 1985-904731	A 19850916
			WO 1985-US1744	A 19850916
			US 1986-849072	A3 19860404
OTHER SOURCE(S):		MARPAT 111:146828		
GI				



AB The carboxyalkyl dipeptides I (W = Q, Q1, Q2, Q3; n = 0, 1; m, p, q = 0, 1, 2; Y = CH2, CH2O, CH2S; Z = Q4, Q5; A = Cl, CF3; D = CH2, CH2CH2, CH2O, CH2S, CH2CONH; G = CONR7(CH2)t, SO2NR7(CH2)t; t = 0, 1; R1, R4 = OH, alkoxy, phenoxyalkoxy, phenylthioalkoxy, etc.; R2, R5, R6 = H, alkyl; R3 =



H, alkyl, aminoalkyl; R7 = H, alkyl, phenylalkyl] are prepared as drugs that reduce intraocular pressure (no biol. data). N-[1(S)-Ethoxycarbonyl-2-(4-nitrophenyl)ethyl]-(S)-alanine (preparation given) was reacted with benzyl cis,syn-octahydro-1H-indole-2(S)-carboxylate, in Et3N-containing DMF, at 0 to -5°, in the presence of 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide-HCl, to give benzyl 1-[N-[1(S)-ethoxycarbonyl-2-(4-nitrophenyl)ethyl]-(S)-alanyl]-cis,syn-octahydro-1H-indole-2(S)-carboxylate, which upon hydrogenation over Pd/C in absolute EtOH gave 1-[N-[1-(S)-ethoxycarbonyl-2-(4-aminophenyl)ethyl]-(S)-alanyl]-cis,syn-octahydro-1H-indole-2(S)-carboxylic acid. A topical solution comprised 1-[N-[1-(S)-ethoxycarbonyl-3-[4-(6-chloro-3,4-dihydro-1,1-dioxo-7-sulfamoyl-2H-1,2,4-benzothiadiazine)acetamidophenyl]propyl]-(S)-alanyl]-cis,syn-octahydro-1H-indole-2(S)-carboxylic acid 10.0, Na2HPO4 10.4, NaH2PO4 2.4, chlorobutanol 5.0, hydroxypropylmethylcellulose 5.0 mg and water to 1 mL. The pH was adjusted to 7.4.

L43 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:497735 HCAPLUS

DOCUMENT NUMBER: 111:97735

TITLE: Preparation of proline- and perhydroindolecarboxylate-containing dipeptides as antihypertensives

INVENTOR(S): Gold, Elijah H.; Neustadt, Bernard R.; **Smith, Elizabeth M.**PATENT ASSIGNEE(S): **Schering Corp., USA**

SOURCE: U.S., 6 pp. Cont.-in-part of U.S. Ser. No. 258,484, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

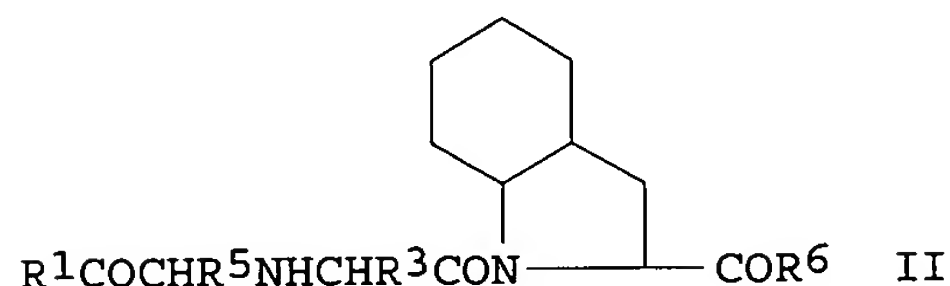
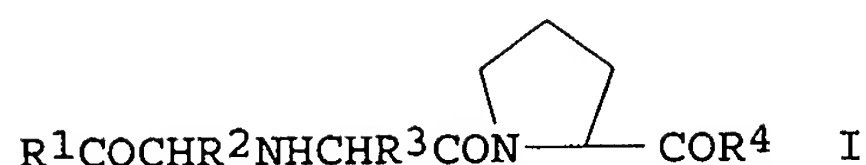
FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4808573	A	19890228	US 1987-29293	19870323
EP 50800	A1	19820505	EP 1981-108348	19811015
EP 50800	B1	19860618		
EP 50800	B2	19950607		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
ZA 8107261	A	19820929	ZA 1981-7261	19811020
US 4818749	A	19890404	US 1987-117008	19871104
PRIORITY APPLN. INFO.:			US 1980-199886	A2 19801023
			US 1980-201649	A2 19801028
			US 1981-258484	A2 19810428
			EP 1981-108348	A 19811015
			US 1981-334053	A2 19811223
			US 1987-29293	A2 19870323

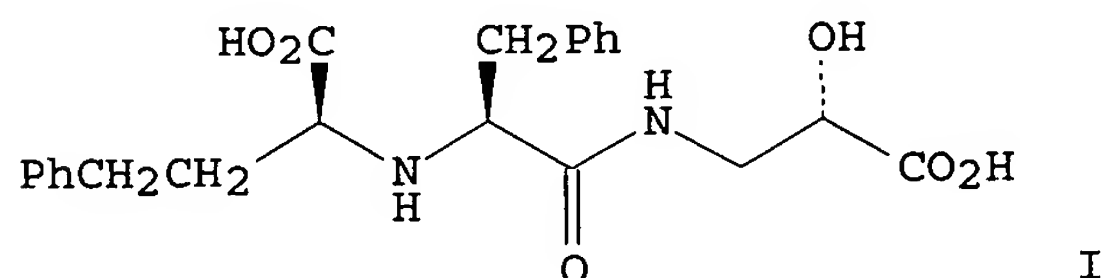
OTHER SOURCE(S): MARPAT 111:97735

GI



AB The title compds. [I and II; R<sub>1</sub>, R<sub>4</sub> = OH, alkoxy; R<sub>2</sub> = PhCH<sub>2</sub>SCH<sub>2</sub>, PhCH<sub>2</sub>CH<sub>2</sub>SCH<sub>2</sub>, naphthylmethylthiomethyl, methylbenzylthiomethyl, 2-(carboxyphenyl)ethyl, 2-(alkoxycarbonylphenyl)ethyl; R<sub>3</sub> = H, alkyl, aminoalkyl; R<sub>5</sub> = benzyloxyalkyl, benzylthioalkyl], useful as angiotensin converting enzyme (ACE) inhibitors (no data), were prepared. A mixture of S-benzyl-L-cysteine Et ester, N-pyruvoyl-L-proline, and 5Å sieves was stirred 2 days in THF. NaBH<sub>3</sub>CN in EtOH was added and the mixture was stirred 18 h to give N-[(1R)-ethoxycarbonyl-2-benzylthioethyl]-(R,S)-alanyl-(S)-proline-HCl.

L43 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1989:173745 HCAPLUS  
 DOCUMENT NUMBER: 110:173745  
 TITLE: Carboxyalkyl dipeptides with atrial natriuretic factor potentiating and antihypertensive activity  
 AUTHOR(S): Haslanger, Martin F.; Sybertz, Edmund J.; Neustadt, Bernard R.; **Smith, Elizabeth M.**; Nechuta, Terry L.; Berger, Joel  
 CORPORATE SOURCE: Dep. Chem. Res., **Schering-Plough** Res., Bloomfield, NJ, 07003, USA  
 SOURCE: Journal of Medicinal Chemistry (1989), 32(4), 737-9  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 110:173745  
 GI



AB Carboxyalkyl dipeptide I was prepared by solution methods. I and related carboxyalkyl dipeptides inhibited neutral endopeptidase (NEP), a protease which inactivates atrial natriuretic factor (ANF) in vitro. These inhibitors of NEP potentiate the hypotensive activity of exogenous ANF and express antihypertensive activity in a rodent model of volume-dependent hypertension. Although the precise role of ANF in the antihypertensive action of I remains to be established, these results suggest that inhibition of NEP represents a novel mechanism by which to reduce arterial blood pressure.

L43 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:448448 HCAPLUS

DOCUMENT NUMBER: 109:48448

TITLE: Neutral metalloendopeptidase inhibitors in the treatment of hypertension, compositions and kits containing the inhibitors, manufacture of the compositions, compounds of the compositions and their preparation

INVENTOR(S): Haslanger, Martin F.; Sybertz, Edmund, Jr.; Neustadt, Bernard R.; Smith, Elizabeth M.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: Eur. Pat. Appl., 167 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

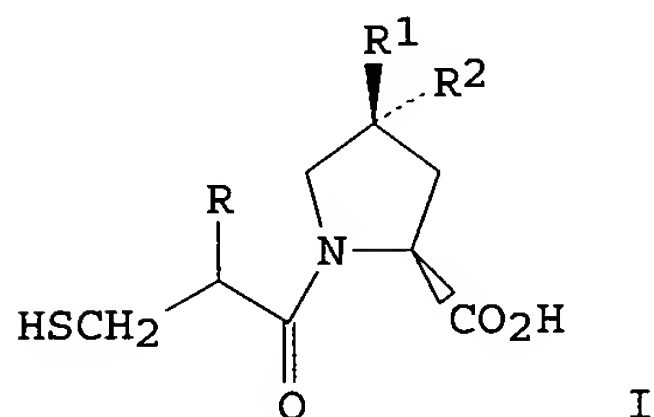
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 254032	A2	19880127	EP 1987-108730	19870617
EP 254032	A3	19900905		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4749688	A	19880607	US 1986-876610	19860620
US 4801609	A	19890131	US 1987-32153	19870327
EP 566157	A1	19931020	EP 1993-107499	19870617
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8702720	A	19871221	FI 1987-2720	19870618
AU 8774458	A1	19871224	AU 1987-74458	19870618
AU 602701	B2	19901025		
ZA 8704413	A	19880224	ZA 1987-4413	19870618
HU 44940	A2	19880530	HU 1987-2786	19870618
IL 82908	A1	19910916	IL 1987-82908	19870618
DK 8703138	A	19871221	DK 1987-3138	19870619
NO 8702589	A	19871221	NO 1987-2589	19870619
JP 63039855	A2	19880220	JP 1987-153219	19870619
JP 2542620	B2	19961009		
JP 08283153	A2	19961029	JP 1995-246555	19870619
US 5061710	A	19911029	US 1987-133669	19871216
AU 9068517	A1	19910718	AU 1990-68517	19901227
AU 636423	B2	19930429		
US 4801609	B1	19931109	US 1991-90002282	19910214
US 5262436	A	19931116	US 1991-741025	19910806
JP 08176100	A2	19960709	JP 1995-246554	19950821
PRIORITY APPLN. INFO.:			US 1986-876610	A 19860620
			US 1987-32153	A 19870327
			EP 1987-108730	A 19870617
			JP 1987-153219	A3 19870619
			US 1987-133669	A3 19871216

OTHER SOURCE(S): MARPAT 109:48448

AB Neutral metalloendopeptidase (NMEP) inhibitor is used alone or combined with an atrial peptide or an angiotensin converting enzyme (ACE) inhibitor for preparation of pharmaceutical compns. for treating hypertension. The compns. are obtained by mixing a NMEP inhibitor, alone or combined with an atrial peptide or ACE inhibitor, with a pharmaceutically acceptable carrier. S-(4-Methylbenzyl)-L-cysteine, Me ester hydrochloride was prepared by adding thionyl chloride dropwise to N-tert-butyloxycarbonyl-S-(4-methylbenzyl)-L-cysteine in MeOH, heating the mixture under reflux for 90 min, cooling to room temperature, and concentrating in vacuo. Rats with induced

hypertension were dosed s.c. with N-(N-[L-1-(2,2-dimethyl-1-oxopropoxy)methoxy]carbonyl)-2-phenylethyl)-L-phenylalanine]- $\beta$ -alanine and 1-[(2S)-3-mercapto-2-methyl-1-oxypropyl]-L-proline in Me cellulose vehicle to give a 1-, 2-, 3-, and 4-h decrease in blood pressure of 14, 19, 19, and 15 mmHg vs. an increase of 14, 11, 11, and 8 with the NMEP inhibitor alone and a decrease of 11, 7, 1, and 1 mmHg with the ACE inhibitor alone.

L43 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1988:438215 HCAPLUS  
 DOCUMENT NUMBER: 109:38215  
 TITLE: Synthesis and pharmacological activity of  
 angiotensin-converting enzyme inhibitors:  
 N-(mercaptoacyl)-4-substituted-(S)-prolines  
 AUTHOR(S): **Smith, Elizabeth M.**; Swiss, Gerald F.;  
 Neustadt, Bernard R.; Gold, Elijah H.; Sommer, Jane  
 A.; Brown, Arthur D.; Chiu, Peter J. S.; Moran, Rosa;  
 Sybertz, Edmund J.; Baum, Thomas  
 CORPORATE SOURCE: Dep. Med. Chem., **Schering-Plough Corp.**,  
 Bloomfield, NJ, 07003, USA  
 SOURCE: Journal of Medicinal Chemistry (1988), 31(4), 875-85  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 109:38215  
 GI



AB Title compds. I (R = R,S-Me, H; R1 = H, OH, OMe, SH, SMe, F, CN, etc.; R2 = H, OH, OMe, F, etc.; R1R2 = OCH2CH2O, SCH2CH2S) were prepared These compds. were evaluated in vitro for inhibition of angiotensin-converting enzyme (ACE), and selected compds. were evaluated in vivo for ACE inhibition. The most potent compds. in vitro are I [R = R,S-Me; R1R2 = OCH2CH2O, OCH2CMe2CH2O, SCH2CH2S, S(CH2)3S; R = H, R1R2 = SCH2CH2S]. The most potent compds. in vivo are I [R = R,S-Me; R1R2 = OCH2CH2O, SCH2CH2S, S(CH2)3S; R = H, R1R2 = SCH2CH2S, S(CH2)3S; R = R,S-Me, R1 = OMe, R2 = H].

L43 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1988:180075 HCAPLUS  
 DOCUMENT NUMBER: 108:180075  
 TITLE: Topical ocular hypotensive effects of the novel  
 angiotensin-converting enzyme inhibitor SCH 33861 in  
 conscious rabbits  
 AUTHOR(S): Watkins, Robert W.; Baum, Thomas; Cedenno, Karen;  
**Smith, Elizabeth M.**; Yuen, Pui Ho; Ahn, Ho  
 Sam; Barnett, Allen  
 CORPORATE SOURCE: Dep. Pharmacol., **Schering Res.**, Bloomfield,  
 NJ, USA  
 SOURCE: Journal of Ocular Pharmacology (1987), 3(4), 295-307

CODEN: JOPHER; ISSN: 8756-3320

DOCUMENT TYPE: Journal

LANGUAGE: English

AB SCH 33861 is a novel, nonsulfhydryl, angiotensin converting enzyme (ACE) inhibitor. Topical administration of the compound to the eye of conscious rabbits was employed to examine actions on intraocular pressure (IOP). Falls in IOP resulted from SCH 33861 (0.001-0.01%) administration. Ocular hypotensive responses were sustained for as long as 24 h following a single application of 0.001% SCH 33861. The RSS isomer of SCH 33861, which is 200-fold weaker an ACE inhibitor than SCH 33861, caused only transient falls in IOP at 0.1% concentration. The magnitude of the fall in IOP induced by 0.001% SCH 33861 (4.8 mmHg) was comparable to that produced by 0.5% timolol (4.5 mmHg). Other ACE inhibitors such as captopril (0.1%) and enalaprilic acid (0.01%) also reduced IOP by 4.0 and 4.7 mmHg, resp. These findings indicate that SCH 33861 is 500-fold more potent on a weight basis than is timolol in lowering IOP. No loss of ocular hypotensive activity was observed when SCH 33861 was administered twice daily for 5 days suggesting little, if any, potential for tolerance development. SCH 33861, as well as the other ACE inhibitors, caused neither ocular irritation nor alteration of pupil diameter. These findings suggest that inhibition of ocular ACE may represent an effective means of reducing IOP.

L43 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1987:440330 HCAPLUS

DOCUMENT NUMBER: 107:40330

TITLE: Preparation of amino acid derivatives as antihypertensive agents, and pharmaceutical compositions containing them

INVENTOR(S): Nevstadt, Bernard Ray; **Smith, Elizabeth Melva**; Magatti, Charles Victor; Gold, Elijah HermanPATENT ASSIGNEE(S): **Schering Corp., USA**

SOURCE: S. African, 50 pp.

CODEN: SFXAB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
ZA 8600083	A	19860827	ZA 1986-83	19860106
PRIORITY APPLN. INFO.:			ZA 1986-83	19860106

GI For diagram(s), see printed CA Issue.

AB The title compds. [I; R = substituted Ph, 2H-1,2,4-benzothiadiazin-3-yl; R1, R4 = OH, (un)substituted alkoxy; R2, R6 = H, alkyl; R3 = H, (amino)alkyl; W = Q1-Q4; Y = CH2, CH2O, CH2S; Z = (CH2)n, CH2O, CH2S, CH2CONH, CONR5(CH2)p, SO2NR5(CH2)p; R5 = H, (phenyl)alkyl; m = 0-2; n = 1, 2; p, z = 0, 1; x, y = 0-2; x + y = 1, 2] were prepared as angiotensin-converting enzyme inhibitors, useful as antihypertensives and in treatment of glaucoma. 4-Nitro-L-phenylalanine Et ester-HCl was N-alkylated with (R)-F3CSO3CHMeCO2CMe3 to give N-[1(S)-(ethoxycarbonyl)-2-(4-nitrophenyl)ethyl]-S-alanine tert-Bu ester. The latter was converted in 5 steps to 1-[N-[1(S)-(ethoxycarbonyl)-2-[4-(4-chloro-3-sulfamoylbenzamido)phenyl]ethyl]-(S)-alanyl]-cis,syn-octahydro-1H-indole-2(S)-carboxylic acid (II). In rats selected I inhibited angiotensin I-induced hypertension with ED50 of 33 µg/kg and 36 µg/kg, i.v. Formulations containing I are given.

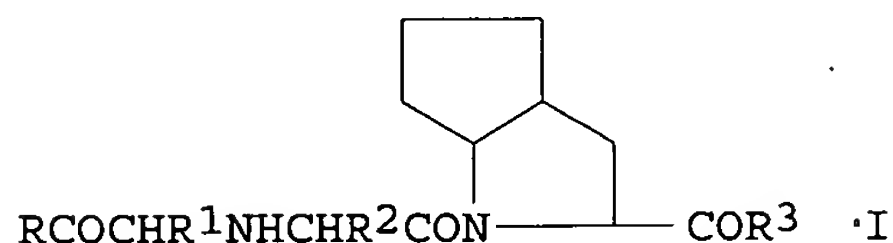
L43 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1986:626337 HCAPLUS

DOCUMENT NUMBER: 105:226337  
 TITLE: cis,endo-Octahydrocyclopenta[b]pyrrole-2-carboxylate  
 INVENTOR(S): Gold, Elijah Herman; Neustadt, Bernard Ray;  
 Smith, Elizabeth Melva  
 PATENT ASSIGNEE(S): Schering Corp., USA  
 SOURCE: PCT Int. Appl., 26 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8600896	A1	19860213	WO 1985-US1406	19850726
W: AU, DK, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4587258	A	19860506	US 1984-635390	19840730
AU 8546718	A1	19860225	AU 1985-46718	19850726
AU 581919	B2	19890309		
JP 61502818	T2	19861204	JP 1985-503359	19850726
DK 8601408	A	19860326	DK 1986-1408	19860326
US 4831157	A	19890516	US 1988-250300	19880928
PRIORITY APPLN. INFO.:			US 1984-635390	A 19840730
			US 1980-199886	A2 19801023
			US 1980-201649	A2 19801028
			US 1981-258484	A2 19810428
			EP 1981-108348	A 19811015
			WO 1985-US1406	A 19850726
			US 1986-817639	A3 19860110

GI



AB The title compds. I (R, R<sub>3</sub> = OH, alkoxy, alkenoxy, aryloxy, aminoalkoxy, etc.; R<sub>1</sub> = H, (un)substituted C<sub>1</sub>-10 alkyl, alkoxy, aryloxy, heteroaryloxy, NH<sub>2</sub>, etc.; R<sub>2</sub> = H, alkyl, Ph, hydroxyphenyl, acylamino, etc.), useful intermediates for angiotensin-converting enzyme inhibitors, were prepared. Thus, 1-[(S)-alanyl]cis-endo-octahydrocyclopenta[b]pyrrole-2(S)-carboxylic acid, prepared in 3 steps from Et cis, endo-octahydrocyclopenta[b]pyrrole-2-carboxylate, in MeOH was condensed with PhCH<sub>2</sub>CH<sub>2</sub>COCOEt to give 1-[N-(1(R,S-carbethoxy-3-phenylpropyl)-(S)-alanyl]-cis,endo-octahydrocyclopenta[b]pyrrole-2(S)-carboxylic acid.

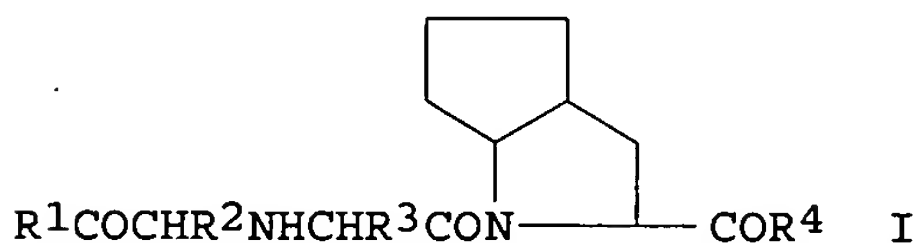
L43 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1986:534346 HCAPLUS  
 DOCUMENT NUMBER: 105:134346  
 TITLE: Peptides as angiotensin-converting enzyme inhibitors  
 INVENTOR(S): Gold, Elijah H.; Neustadt, Bernard R.; Smith,  
 Elizabeth M.  
 PATENT ASSIGNEE(S): Schering Corp., USA  
 SOURCE: U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 258,484.  
 CODEN: USXXAM



DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4587258	A	19860506	US 1984-635390	19840730
EP 50800	A1	19820505	EP 1981-108348	19811015
EP 50800	B1	19860618		
EP 50800	B2	19950607		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
ZA 8107261	A	19820929	ZA 1981-7261	19811020
WO 8600896	A1	19860213	WO 1985-US1406	19850726
W: AU, DK, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8546718	A1	19860225	AU 1985-46718	19850726
AU 581919	B2	19890309		
EP 190224	A1	19860813	EP 1985-903779	19850726
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 61502818	T2	19861204	JP 1985-503359	19850726
ZA 8505659	A	19870325	ZA 1985-5659	19850726
CA 1244041	A1	19881101	CA 1985-487583	19850726
DK 8601408	A	19860326	DK 1986-1408	19860326
US 4831157	A	19890516	US 1988-250300	19880928
PRIORITY APPLN. INFO.:			US 1980-199886	A2 19801023
			US 1980-201649	A2 19801028
			US 1981-258484	A2 19810428
			EP 1981-108348	A 19811015
			US 1984-635390	A 19840730
			WO 1985-US1406	A 19850726
			US 1986-817639	A3 19860110

OTHER SOURCE(S): CASREACT 105:134346  
 GI



AB Proline derivative peptides I (R1 and R4 are OH, alkoxy, alkenyloxy, NH2, mono- or dialkylamino, etc.; R2 = H, alkyl, hydroxyalkyl, aminoalkyl, indolylalkyl, aralkyl, etc.; R3 = H, alkyl, phenylalkyl, hydroxyalkyl, aminoalkyl, etc.) were prepared, and they are useful in the treatment of glaucoma (no data). I (R1 = OEt, R2 = PhCH2CH2, R3 = Me, R4 = OH) was prepared in a series of reactions.

L43 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1986:479362 HCAPLUS

DOCUMENT NUMBER: 105:79362

TITLE: Alanylindole antihypertensive agents

INVENTOR(S): Doll, Ronald J.; Neustadt, Bernard R.; Smith, Elizabeth M.; Magatti, Charles V.; Gold, Elijah H.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 500,494,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

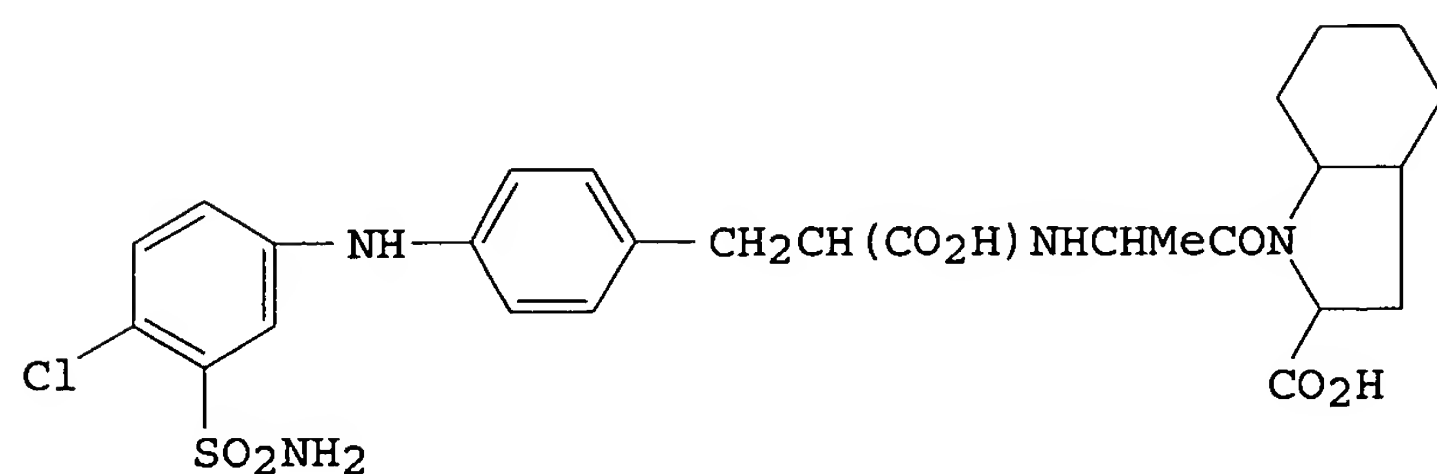
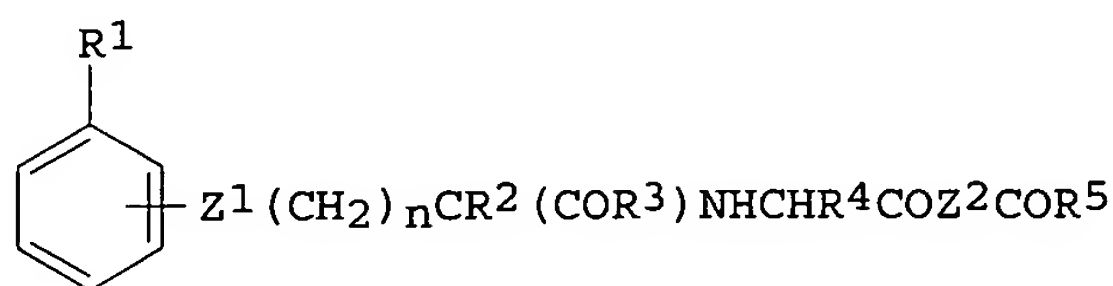
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4584285	A	19860422	US 1984-651378	19840917
WO 8701707	A1	19870326	WO 1985-US1744	19850916
W: AU, FI, HU, JP, KR, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8548088	A1	19870407	AU 1985-48088	19850916
AU 581929	B2	19890309		
EP 236307	A1	19870916	EP 1985-904731	19850916
EP 236307	B1	19910417		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
HU 43620	A2	19871130	HU 1985-4245	19850916
HU 199507	B	19900228		
JP 63500938	T2	19880407	JP 1985-504147	19850916
AT 62694	E	19910515	AT 1985-904731	19850916
IL 77451	A1	19900712	IL 1985-77451	19851226
CA 1276396	A1	19901113	CA 1986-499291	19860109
US 4691049	A	19870901	US 1986-831383	19860220
US 4783444	A	19881108	US 1986-849072	19860404
FI 8702110	A	19870513	FI 1987-2110	19870513
NO 8701982	A	19870513	NO 1987-1982	19870513
US 4840772	A	19890620	US 1988-227954	19880803
PRIORITY APPLN. INFO.:				
			US 1983-500494	A2 19830602
			US 1984-651378	A 19840917
			EP 1985-904731	A 19850916
			WO 1985-US1744	A 19850916
			US 1986-849072	A3 19860404

OTHER SOURCE(S):

CASREACT 105:79362

GI



AB Amino acid derivs. I [R1 = benzothiadiazinylalkyl, chloro(sulfamoyl)benzamido, etc.; Z1 = CH2, CH2O, CH2S; n = 0-2; R2 = H, alkyl; R3, R5 = OH, alkoxy, etc.; R4 = H, alkyl, aminoalkyl; Z2 = proline

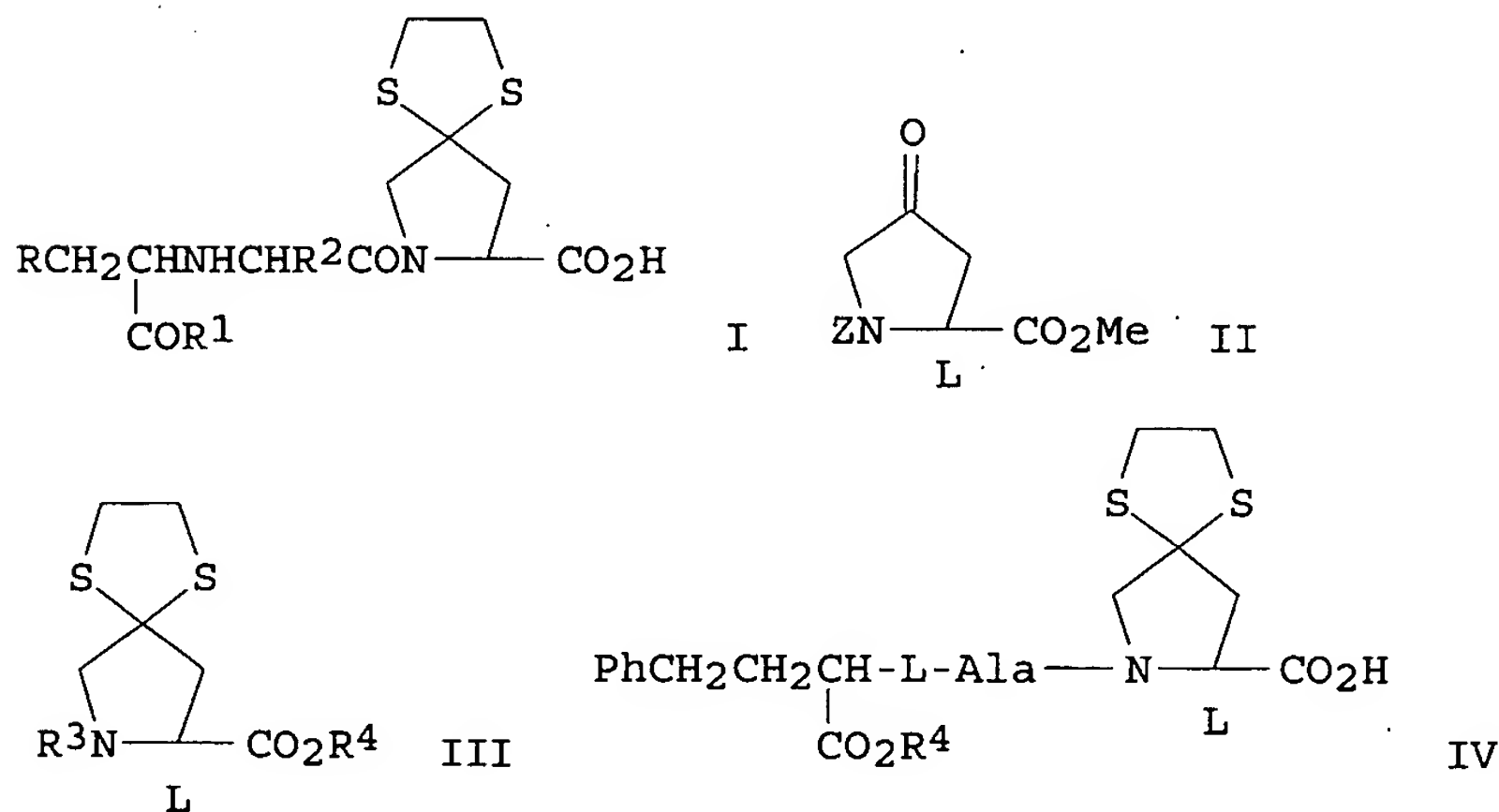


residue, octahydroindole analog, etc.] were prepared, and they are useful as antihypertensives (no data). Alanine derivative II was prepared from the reaction product of 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>Et·HCl and BrCHMeCO<sub>2</sub>CMe<sub>3</sub> in a series of reactions.

L43 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1985:96083 HCAPLUS  
 DOCUMENT NUMBER: 102:96083  
 TITLE: 7-Carboxyalkylaminoacyl-1,4-dithia-7-azaspiro[4.4]nonane-8-carboxylic acids  
 INVENTOR(S): Gold, Elijah H.; Neustadt, Bernard R.; Smith, Elizabeth M.  
 PATENT ASSIGNEE(S): Schering Corp., USA  
 SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 258,484.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4470972	A	19840911	US 1982-446929	19821206
ZA 8107261	A	19820929	ZA 1981-7261	19811020
US 5348944	A	19940920	US 1988-261815	19880404
PRIORITY APPLN. INFO.:			US 1980-199886	A2 19801023
			US 1980-201649	A2 19801028
			US 1981-258484	A2 19810428

OTHER SOURCE(S): CASREACT 102:96083  
 GI



AB Title compds. I (R = alkyl, PhCH<sub>2</sub>, PhCH<sub>2</sub>S, PhCH<sub>2</sub>O, PhS, PhO; R<sub>1</sub> = OH, alkoxy; R<sub>2</sub> = H, alkyl, aminoalkyl) were prepared as antihypertensives (no sp. data). Thus, 4-oxo-L-proline II (Z = PhCH<sub>2</sub>O<sub>2</sub>C) was treated with HSCH<sub>2</sub>CH<sub>2</sub>SH in HOAc containing p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H to give 1,4-dithia-7-azaspiro[4.4]nonane III (R<sub>3</sub> = Z, R<sub>4</sub> = Me), which was Z-deblocked by HBr/HOAc to give III.HBr (R<sub>3</sub> = H, R<sub>4</sub> = Me), which was condensed with

Z-L-Ala-ONSu (NSu = succinimido) to give III (R3 = Z-L-Ala, R4 = Me). The latter was saponified to give III (R3 = Z-L-Ala, R4 = H), which was Z-deblocked by HBr/HOAc to give III.HBr (R3 = H-L-Ala, R4 = H). The latter underwent reductive alkylation with PhCH<sub>2</sub>CH<sub>2</sub>COCO<sub>2</sub>Et in the presence of NaBH<sub>3</sub>CN to give title compound IV (R4 = Et), which was saponified to give IV (R4 = H).

L43 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1984:407052 HCAPLUS  
 DOCUMENT NUMBER: 101:7052  
 TITLE: Benzoquinolinones  
 INVENTOR(S): **Smith, Elizabeth Melva**; Doll, Ronald James;  
 Neustadt, Bernard Ray  
 PATENT ASSIGNEE(S): **Schering Corp., USA**  
 SOURCE: Eur. Pat. Appl., 49 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 102046	A1	19840307	EP 1983-108240	19830822
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4511569	A	19850416	US 1982-411764	19820826
US 4474786	A	19841002	US 1983-505050	19830616
JP 59059665	A2	19840405	JP 1983-156220	19830826
PRIORITY APPLN. INFO.:			US 1982-411764	A 19820826
			US 1983-505050	A 19830616

OTHER SOURCE(S): CASREACT 101:7052  
 GI For diagram(s), see printed CA Issue.  
 AB Fused pyridinones I [R = H, alkyl; R1 = H, OH, alkoxy, cyano, alkyl, halo, (un)substituted amino or carbamoyl, acylamino, CO<sub>2</sub>H, esterified CO<sub>2</sub>H, CSNH<sub>2</sub>, C(:NH)NH<sub>2</sub>; Z = CH:CH, (CH<sub>2</sub>)<sub>n</sub> (n = 1-4), (CH<sub>2</sub>)<sub>p</sub>S(O)<sub>m</sub>(CH<sub>2</sub>)<sub>r</sub> or (CH<sub>2</sub>)<sub>p</sub>O(CH<sub>2</sub>)<sub>r</sub> (m = 0, 1, 2; p and r are 0-3); Z1 forms an optionally substituted fused benzo or pyrido], useful as cardiovascular agents (no data), were prepared 1-[(Dimethylamino)methylene]-2-tetralone was treated with NCCH<sub>2</sub>CONH<sub>2</sub> and NaOMe and DMF at 80° to give I (R = H, R1 = cyano, Z = CH<sub>2</sub>CH<sub>2</sub>, Z1 = benzo).

L43 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1984:175294 HCAPLUS  
 DOCUMENT NUMBER: 100:175294  
 TITLE: Carboxyalkyl dipeptides and pharmaceutical compositions containing them  
 INVENTOR(S): **Smith, Elizabeth M.**; Witkowski, Joseph T.;  
 Doll, Ronald J.; Gold, Elijah H.; Neustadt, Bernard R.; Yehaskel, Albert S.  
 PATENT ASSIGNEE(S): **Schering Corp., USA**  
 SOURCE: Eur. Pat. Appl., 134 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 88350	A1	19830914	EP 1983-102014	19830302

## Ward 10\_663042-inventor search

EP 88350	B1	19850220		
R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE				
US 4431644	A	19840214	US 1982-355638	19820308
US 4431645	A	19840214	US 1982-355639	19820308
ZA 8300362	A	19840926	ZA 1983-362	19830119
AT 11921	E	19850315	AT 1983-102014	19830302
NO 8300737	A	19830909	NO 1983-737	19830303
AU 8312035	A1	19830915	AU 1983-12035	19830303
AU 557795	B2	19870108		
GB 2117777	A1	19831019	GB 1983-5837	19830303
GB 2117777	B2	19850626		
ES 520261	A1	19840401	ES 1983-520261	19830303
DK 8301101	A	19830909	DK 1983-1101	19830304
JP 58162561	A2	19830927	JP 1983-35707	19830304
FI 8300752	A	19830909	FI 1983-752	19830307
HU 29605	O	19840228	HU 1983-781	19830307
HU 195520	B	19880530		
ZA 8301844	A	19840627	ZA 1983-1844	19830316
PRIORITY APPLN. INFO.:			US 1982-355638	A 19820308
			US 1982-355639	A 19820308
			US 1982-360532	A 19820322
			ZA 1983-362	A 19830119
			EP 1983-102014	A 19830302

OTHER SOURCE(S): CASREACT 100:175294

GI For diagram(s), see printed CA Issue.

AB Title compds. RCH<sub>2</sub>CR<sub>1</sub>(CO<sub>2</sub>H)-NHCH[(CH<sub>2</sub>)<sub>n</sub>XR<sub>2</sub>]CO-X<sub>1</sub>-OH [R = alkyl, PhCH<sub>2</sub>, PhCH<sub>2</sub>O, PhCH<sub>2</sub>S, PhO, PhS; R<sub>1</sub> = H, alkyl; X = S, R<sub>2</sub> = substituted (3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazin-3-yl 1,1-dioxide) methyl; X = NR<sub>3</sub> (R<sub>3</sub> = H, alkyl, Ph), R<sub>2</sub> = sulfamoyl-substituted Bz, PhSO<sub>2</sub>, or benzyl; XR<sub>2</sub> = sulfamoyl-substituted N-containing heterocyclic ring; n = 1-6; X<sub>1</sub> = (un)substituted Pro or related N-containing heterocyclic amino acid residues] were prepared as antihypertensives and agents for the treatment of congestive heart failure and glaucoma (no data). Thus, H-L-Lys(Z)-OH (Z = CO<sub>2</sub>CH<sub>2</sub>Ph) was treated with PhCH<sub>2</sub>CH<sub>2</sub>COCO<sub>2</sub>Et and NaBH<sub>3</sub>CN to give (S)-PhCH<sub>2</sub>CH<sub>2</sub>CH(CO<sub>2</sub>Et)-L-Lys(Z)-OH, which was condensed with indole I to give dipeptide II (R<sub>4</sub> = Z, R<sub>5</sub> = CH<sub>2</sub>Ph), which was deblocked by hydrogenolysis to give II (R<sub>4</sub> = R<sub>5</sub> = H), which was sulfonylated with 4-chloro-3-sulfamoylbenzenesulfonyl chloride to give title compound III.

L43 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1982:616730 HCAPLUS

DOCUMENT NUMBER: 97:216730

TITLE: Carboxyalkyl dipeptides and pharmaceutical compositions containing them

INVENTOR(S): Neustadt, Bernard R.; Gold, Elijah H.; **Smith, Elizabeth M.**PATENT ASSIGNEE(S): **Schering Corp., USA**

SOURCE: Eur. Pat. Appl., 123 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

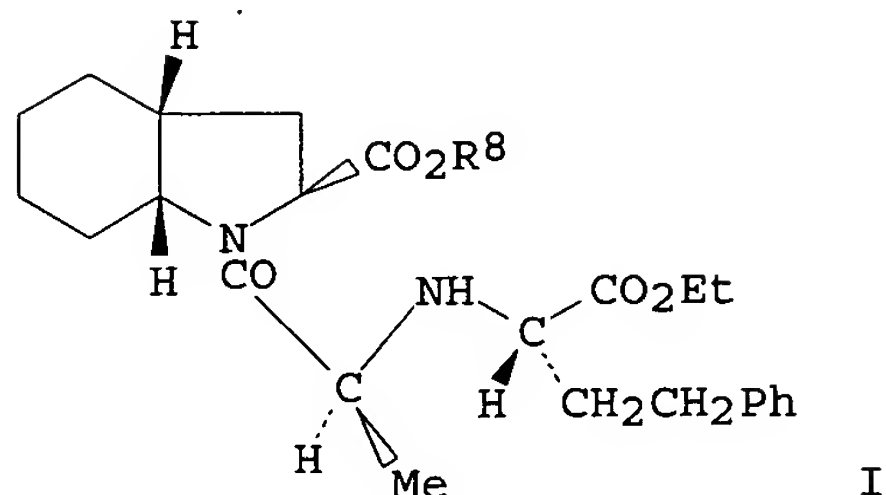
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 50800	A1	19820505	EP 1981-108348	19811015
EP 50800	B1	19860618		
EP 50800	B2	19950607		

R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE

## Ward 10\_663042-inventor search

AT 20469	E	19860715	AT 1981-108348	19811015
DK 8104625	A	19820424	DK 1981-4625	19811020
DK 161523	B	19910715		
DK 161523	C	19911223		
FI 8103283	A	19820424	FI 1981-3283	19811020
FI 83222	B	19910228		
FI 83222	C	19910610		
AU 8176614	A1	19820429	AU 1981-76614	19811020
AU 554362	B2	19860821		
ZA 8107261	A	19820929	ZA 1981-7261	19811020
NO 8103546	A	19820426	NO 1981-3546	19811021
NO 164983	B	19900827		
NO 164983	C	19901205		
JP 57112359	A2	19820713	JP 1981-168511	19811021
JP 01032240	B4	19890629		
ES 506414	A1	19831001	ES 1981-506414	19811021
IL 64085	A1	19861231	IL 1981-64085	19811021
HU 32785	O	19840928	HU 1981-3078	19811022
HU 193146	B	19870828		
US 4587258	A	19860506	US 1984-635390	19840730
US 4808573	A	19890228	US 1987-29293	19870323
US 4818749	A	19890404	US 1987-117008	19871104
US 4831157	A	19890516	US 1988-250300	19880928
JP 01163197	A2	19890627	JP 1988-283542	19881109
PRIORITY APPLN. INFO.:			US 1980-199886	A 19801023
			US 1981-258484	A 19810428
			US 1980-201649	A2 19801028
			EP 1981-108348	A 19811015
			US 1981-334053	A2 19811223
			US 1984-635390	A2 19840730
			WO 1985-US1406	A 19850726
			US 1986-817639	A3 19860110
			US 1987-29293	A2 19870323

GI



AB RCOCR<sub>1</sub>R<sub>2</sub>NHCHR<sub>3</sub>CONR<sub>4</sub>CR<sub>5</sub>R<sub>7</sub>COR<sub>6</sub> [R, R<sub>6</sub> = OH, (un)substituted alkoxy, alkenyloxy, (un)substituted NH<sub>2</sub>; R<sub>1</sub> = H, (un)substituted alkyl; R<sub>2</sub>, R<sub>7</sub> = H, (un)substituted alkyl; R<sub>3</sub> = H, (un)substituted alkyl, (un)substituted phenylalkyl; R<sub>4</sub>, R<sub>5</sub> = H, (un)substituted alkyl; R<sub>4</sub>R<sub>5</sub> form ring systems] were prepared as antihypertensives and angiotensin-converting enzyme inhibitors (no data). Thus, H-L-Ala-OCH<sub>2</sub>Ph tosylate was treated with PhCH<sub>2</sub>CH<sub>2</sub>COCO<sub>2</sub>Et and reduced with NaBH<sub>3</sub>(CN) and then debenzylated by hydrogenolysis to give (S)-PhCH<sub>2</sub>CH<sub>2</sub>CH(CO<sub>2</sub>Et)-L-Ala-OH. The latter was condensed with cis,syn-octahydroindole-2(S)-carboxylic acid benzyl ester to give indole I (R<sub>8</sub> = CH<sub>2</sub>Ph), which was debenzylated by hydrogenolysis to give I (R<sub>8</sub> = H).

L43 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1975:73298 HCAPLUS  
DOCUMENT NUMBER: 82:73298  
TITLE: Thermal and photolytic rearrangement of  
4,6-unsaturated 4-azido-3-ketosteroids to  
6-unsaturated 5 $\beta$ -cyano-A-nor-3-ketosteroids  
AUTHOR(S): **Smith, Elizabeth M.**; Shapiro, Elliot L.;  
Teutsch, George; Weber, Lois; Herzog, Hershel L.;  
McPhail, Andrew T.; Tschang, Pui-Sen Wong; Meinwald,  
Jerrold  
CORPORATE SOURCE: Nat. Prod. Res. Dep., **Schering Corp.**,  
Bloomfield, NJ, USA  
SOURCE: Tetrahedron Letters (1974), (39), 3519-22  
CODEN: TELEAY; ISSN: 0040-4039  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI For diagram(s), see printed CA Issue.  
AB Thermal and photochem. ring contraction of the 4-azidoketo steroids I (X =  
X1 = H2, R2R3 = O or R2 = OAc, R3 = H; X = H2, X1 = CH2, R2 = MeCO, R3 =  
OAc; X = O, X1 = H2, R2 = AcOCH2CO, R3 = OH) gave the corresponding  
5 $\beta$ -cyano-A-norsteroids II. The structure of II (X = X1 = H2, R2R3 =  
O) was confirmed by x-ray anal. The orthorhombic crystals, space group  
P212121, had a 11.70, b 12.89, c 10.89, and Z = 4. The structure was  
solved by direct phase determining procedures and refined by full-matrix  
least-squares calcns. to R 0.107 for 1282 reflections.

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